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SCIENTIFIC EXPERIMENT AND MEDICINE[1]

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MODERN medicine presents many aspects. Its fields of influence and interest have expanded into a mighty domain with the passing of the centuries. The varied and increasingly significant activities therein now awaken the concern not only of the practitioner but also of the layman. Public health and preventive medicine have become problems for the state as well as the individual citizen. A century ago the distinguished physician Laënnec asserted, with what was perhaps an exaggerated modesty, that "the aim of medicine is the cure of disease." He promptly added that this end might be attained in a multitude of ways, among which was a consideration of the nature of diseases.

The medicine of to-day is no longer satisfied with a program limited primarily to practical therapy. New enthusiasms have been developed. In discussing the changes of view-point that have been instituted in recent years, A. E. Cohn[2] remarked:

> We should perhaps add, by way of interpreting or perhaps of supplementing Laënnec's meaning, that we believe it necessary as the basis of therapeutics to understand the mechanisms, that is to say, the processes which underlie the manifestations of disease, for it is these which it is one of our functions to attempt to correct. That is our practical aim. We have learned a lesson also in another direction. It is that, as in other disciplines, learning may be pursued for its own sake. And the reason for this is twofold. Men have learned that the direct is not always the shortest road to the attainment of their objects. It is true that results, ultimately of practical value, have issued from disinterested learning. But this argument still is based on utility and leaves many persons imbued with natural curiosity with-

[1] The Alpha Omega Alpha lecture, delivered at New Orleans, May, 1932.

[2] A. E. Cohn, *Jour. Clin. Investigation*, 1: 1, 1924; also "Medicine, Science and Art," University of Chicago Press, Chicago, 1931.

out enthusiasm. It is perhaps not unfair to say that these disinterested students have not been made welcome in medicine as they have been in other departments of learning. And this is a defect in our organization even if it represents no defect in our conceptions. The problems of disease offer legitimate objects of inquiry, as do problems in physiology, and may be pursued in the same spirit. The illumination which has resulted from study of this kind requires no defense. Its value in the development of science is sufficiently established [p. 128].

This spirit seems to be recognized in the functions of the Alpha Omega Alpha Medical Honor Society. Its definite mission, we are reminded, is "to encourage personal honesty and the spirit of medical research." Some of my predecessors in this lectureship have discussed present-day problems of medical ethics and programs of professional conduct before you. I sometimes wonder why it should seem desirable, if not actually necessary, to attempt to frame specific codes of ethics for the various professions; why human duty should not be reasonably clear to all educated persons and applicable with comparable convictions in all walks of human endeavor. Hence my interest in a statement in the address of the Hon. Ray Lyman Wilbur[3] at the annual meeting of the Alpha Omega Alpha in Washington, 1927. He said:

> In the profession there are a number of traditionalists to whom ritualism, etiquette and ethics are all apt to mean the same thing. There are some who have tried to hold back the advancing tides of medicine by an appeal to the principles of ethics as a method of controlling the more rapidly advancing members of the profession. They have called on the voice of the past and on authority, forgetting, as Dr. John Scotus has said, that "authority springs from reason, not reason from authority."

The "mores" of our modern society and its practice of ethics are far more likely to be motivated by human experience and the necessities of social intercourse than by the formulated dictates of groups of men.

The practicing physician, as well as the special investigator whose highest development this society ventures to promote, inevitably assumes a large burden of responsibility for the further development of medical knowledge in behalf of human welfare. The progressive devotee of medicine, notably in the earlier days, has received his inspiration from whatever opportunities were presented to him. The great chance came to our pioneer American physiologist, Dr. William Beaumont—the "backwoods physiologist," as Sir William Osler named him—in the frontier of Northern Michigan in the days when it was far away from any medical center. Beaumont quickly realized the unique opportunity that his patient, Alexis St. Martin, afforded to advance our understanding of gastric functions; and the army surgeon promptly took advantage thereof in a series of observations and experiments that are familiar to every student of medicine. To-day we marvel at Beaumont's accomplishments that were developed not in the midst of well-equipped laboratories or with the aid of brilliant mentors, but rather through his own ingenuity and persistent effort in the outposts of early American civilization. Chance observation constituted the first step in Beaumont's discoveries; and he exemplified the saying attributed to Pasteur that "in the field of observation the chance comes only to the mind that is prepared."[4]

Progress would indeed be slow in these days if it were dependent solely upon studies of the natural or accidental deviations from the routine of life. "Medicine," L. J. Henderson[5] reminds us, "has passed through the empirical, the systematic, the nosological and the morphological stages and has entered upon the experimental stage. Thus it has finally become physiological, for physiology is the larger part of experimental medicine." As F. S. Lee[6] has pointed out,

> Ancient medicine is characterized preëminently by philosophical speculation and empiricism; modern medicine by experimentation. The ancient physician was content to observe phenomena as they existed under their natural conditions, to interpret them in accordance with a philosophical system, and to treat disease in the light of what his system and past experience had taught him. The modern physician does not rely on a philosophical system. Like his forerunner, however, he, too, observes phenomena under their natural conditions; but he goes further than this and alters the conditions, and thus he obtains an alteration of the phenomena and a new standpoint from which to view them. He may apply to the cure of disease past experience, it is true, but it is past experience that has been put to the test of modern experiment. Moreover, by the aid of further experiment he pushes out into the unknown, sees disease from unusual standpoints, and devises new and hitherto unsuspected methods of dealing with it. If he forms a working hypothesis, it, too, has to be submitted to experimentation, for to-day men of medicine have little patience with a new idea that has no experimental evidence in its favor. . . . We can voluntarily control nature's phe-

[3] R. L. Wilbur, "The Honor System in Medical Practice," *Jour. Am. Med. Assn.*, 89: 569, August 20, 1927.

[4] "Dans les champs de l'observation le hasard ne favorise que les esprits préparés." These words are inscribed on the new buildings of the Cambridge Medical School, in England.

[5] L. J. Henderson, in the introduction to the translation of Claude Bernard's "Experimental Medicine," the Macmillan Company, New York, 1927.

[6] F. S. Lee, "Scientific Features of Modern Medicine," Columbia University Press, New York, 1911.

nomena in a great variety of ways; we can control their beginning, their progress, and their ending; and in this way we can make them more accessible to observation. This is the essence of experimentation. It is the voluntary control or modification of natural phenomena. It is an artificial aid to simple observation. By means of it we can penetrate more rapidly and more deeply into nature's secrets than it would ever be possible for us to go unaided.

It is often not only possible but also feasible and proper to undertake scientific experiments on man. Investigation of physiological functions in health and disease, that is, under normal and abnormal conditions, would proceed slowly at best if it were dependent solely upon studies of the human species. Many manifestations of the organism would entirely elude us if we could not create artificially the situations that bring forth the phenomena. Beaumont's observations through the gastric fistula of the volunteer patient St. Martin, for example, raised as many questions as they answered. But cases of gastric fistula were among the extreme rarities of medicine; hence endeavors were made by the Russian investigator Bassow and the French observer Blondlot, almost simultaneously, to imitate the process by art. The methods of producing gastric fistulas in animals by surgical intervention have gradually been highly perfected and have made it possible to expand greatly our knowledge of alimentary functions.

You are well aware that opposition to the use of animals for scientific purposes is voiced in some quarters. As Lee has pointed out, this opposition sometimes wilfully denies the value of animal experimentation in scientific progress; it sometimes assumes the extreme and ethically indefensible attitude of denying the right of man to use animals at all as experimental objects; and it has as its practical aim the establishment of legal restrictions against the practice. It is surely unnecessary in this presence to defend the cause of animal experimentation. The study of the history of medicine as well as your personal experiences must have developed in you the inescapable conviction that the investigation of the physical processes alike in the healthy and the diseased body—the fundament of scientific medicine—can not dispense with occasional experiments on the living animal. They are quite as essential as are admittedly the anatomical examination of the organs of the cadaver, the chemical analysis of its tissues or the physical measurements that have biological import.

Nearly half a century ago my distinguished teacher, Rudolf Heidenhain, of Breslau, offered a cogent retort to the skeptics of that period. It applies with equal or even greater force to-day. "Let us assume," Heidenhain remarked, "that the opponents of animal experimentation were given the right of censorship over all physiological publications, and that a conscientious censor would obliterate with printer's ink all the statements in a text-book of physiology that are based on facts derived from experiments on animals. Such a censored volume," he added, "would have a strange appearance: half of the text would be expunged under the blackness of the ink; while the remainder would then become for the most part unintelligible."

A recent review by Dr. Maurice C. Hall[7] of the humane work of some of our governmental agencies includes a forceful defense of the experimental method. He states:

> The world at large knows and appreciates the combat forces of the practicing physician and veterinarian. It understands that the materials for drugs are collected from far and wide and manufactured for the use of these combat forces. But it knows little of the research or the intelligence service that studies the forces of death and disease and plans new weapons. Now and then it learns from the press that a Lazear has died in a heroic proof that a certain mosquito carries the deadly yellow fever, that the field forces of the Public Health Service have lost three workers to the Rocky Mountain spotted fever with which they worked, that Francis and Lake have contracted the tularemia they were investigating, or that some courageous experimenter with radium has yielded an arm to the enemy on which he spied. For a moment a glimmer of appreciation of these soldiers of the secret service rises in the reader, but this soon dies down, and, when some fanatical opponent of this service approaches him with the tale that all such work has led to no result whatever, he carelessly puts his name to a petition that the laboratories be closed, and in so doing votes that disease and death be allowed to work their way with man and animal except as they may be fought with yesterday's weapons.
>
> Foremost of those who would close the search for knowledge and write "Finis" to the rapidly growing book of medical science is the group of men and women who call themselves antivivisectionists. About a nucleus of paid propagandists clusters this medley of kindly but poorly informed humanitarians, enemies of all medical science, sadists who conceal under an outward love of animals a cruelty towards mankind, persons who boldly flaunt the conviction that they would rather see a child die of disease than have a guinea-pig subjected to experiment to find a way to save the child, persons who admit that they would rather see a million dogs die from parasitism at nature's hands than have a hundred dogs

[7] M. C. Hall, "The Prevention of Cruelty and the Work of a Great Humane Society," *Sci. Monthly*, 34: 211, March, 1932.

subjected to studies on that parasitism by scientists to save the million dogs, and persons whose qualification for passing judgment on medical work is the qualification of an advertising man, a minister, a poet, an author or an actress. This group is the outstanding group of nature's allies in the fight between man and nature's forces of disease and death. They are the enemy aliens who would blow up our laboratories and our ammunition plants, who would cut our service of supplies to the firing line, and who would leave our fighting forces to oppose to the incessant fire of nature's forces the ancient and rusty weapons of Hippocrates and Dioscorides. They do not hesitate to declare the immeasurable services of a Pasteur things of no value; they do not hesitate to tell the medical man and veterinarian who have seen the deaths and suffering of rabies that there is no such thing as rabies; they do not hesitate to tell us who in childhood saw innumerable persons with faces scarred with smallpox pits and who now rarely or never see such faces, that vaccination is a crime. Year after year these persons hear the evidence of the benefits to mankind and to animals from experiments on animals and, year after year, with characteristic intellectual dishonesty, they reiterate the falsehood that no benefits ever came from experiments on animals. It means nothing to them that the disease and death which man deliberately inflicts on a hundred guinea-pigs or dogs to-day save the health and lives of a million persons or dogs or cows next year or in the next ten years. They cast their lot with nature's cruelties and disease and premature death on a large scale; the medical man and scientist cast their lot with man for the frustration of nature's cruelties and the prevention of disease and premature death on the large scale of nature. The antivivisectionists shut their eyes to nature's cruelties; they are not so concerned that man and animals suffer, but they are eager to lay their heavy hands on the work of scientists and to choke to death the sources of information as to how nature fights man and how man may best fight nature.

There are to-day not a few physicians as well as other friends of medicine who, although admitting the noteworthy contributions of animal experimentation, nevertheless urge that its dominant importance is passing. They refer to "laboratory work" as a current fashion, and evanescent as many fads are likely to be. Most fashions, however, leave something of permanent interest or value in their wake. Though the pendulum of enthusiasm for this or that laboratory innovation may at times swing too far, it soon reaches a stable level.

The adverse comments should, however, not be utterly disregarded; and this is specifically true of criticisms of physiological research that have recently been voiced by a distinguished British surgeon. The remarks[8] attributed to him have started a controversy that is in danger of being directed *ad hominem* rather than to the merits of the claims at issue. The surgeon complained, we are told, that "physiologists were neglecting research on man ('hominal research') and were concerned too much with research on animals; that their aloofness from medicine was increasing year by year, and that their discoveries were becoming of less use to the clinician. . . . He characterized as amusing the assumption that ready-made weapons are fashioned in the laboratory and handed over with magisterial authority to the physician, who humbly acquiesces in their prescribed use. As to surgery, he pointed out that the advances in knowledge of gastric and duodenal ulcer and cholelithiasis had been made by surgeons with little help from the laboratory. Indeed, the contribution of the laboratory to the surgery of the stomach was not only almost negligible but was potentially dangerous, because so divergent from human experience. . . . Physiology was too concerned with mice and too little concerned with men."

We may admit freely at the outset, I think, that man himself still offers a fertile field for research. Much of our investigation of man, as well as animals, has been too exclusively concerned with isolated functions; too negligent of the possible integrations of these functions as they concern the physician in his contacts with the human individual as a whole. Perhaps that is why some of the critics complain that current research is often quite futile, or at any rate that it lacks medical utility.

In an exposition of the part played by physiology in the study of disease, the late Dr. D. Noël Paton, of Glasgow, wrote:

> The object of the physiologist must be to attempt to solve all the problems of the way in which living matter acts without considering whether the knowledge may be of use to humanity. At present I fear there is a great tendency to insist that all investigations shall have a utilitarian object; but all experience has shown that most of the important advances in the application of science to medicine have been based upon investigations which primarily seemed to have no direct bearing on the well-being of mankind.[9]

When these words were written in 1919 charges of the inability of physiology to meet the needs of the clinician and of the failure on the part of the physiological teacher were being made as to-day. Paton ventured to believe that

> not infrequently the fault lies not with the physiological teacher but with the hospital physician under whom the student finds himself. The physician, after an inadequate study of the science of physiology in the remote

[8] "Criticism of Physiologic Research," Foreign Letters, *Jour. Am. Med. Assn.*, 96: 203, January 17, 1931.

[9] "Physiology and National Needs," edited by W. D. Halliburton, E. P. Dutton and Co., New York, 1919.

past, may have lost all touch and all sympathy with the science of to-day, may have sunk into an easy empiricism, and may be content to cloak his ignorance by sneers at the application of scientific methods to practice.

Lest I be accused of being an unfair protagonist because my own interests have been centered primarily in the laboratories of the biological sciences, let me turn briefly to the views of clinical investigators. How do they regard or approach the problems of the man in sickness? The objects of the American Society for Clinical Investigation are defined as "the cultivation of clinical research by the methods of the natural sciences; the unification of science and the practice of medicine; the encouragement of scientific investigation by the practitioner, and the diffusion of a scientific spirit among its members." In his presidential address before this society my colleague, Dr. Francis G. Blake,[10] insisted that clinical investigation "should not concern itself primarily with physiology, or chemistry, with physics, mathematics, or biology, nor even with the application of these subjects by the physiologist, or chemist, or physicist or biologist to the problems of clinical medicine, but primarily with the study of the phenomena of disease in all its varied aspects through intimate and constant contact with disease in the field—whether this be in the home, the office, the outpatient clinic, or the wards of the hospital should matter little, provided the contact be comprehensive enough to give a reasonably complete picture of the disease in question."

By this frank statement Blake by no means desires to imply that the so-called experimental method is either inferior or superior to the observational and descriptive procedures; his argument is merely in defense of a method of study that seems to have lost some of its popularity. Blake insists that the inductive experiment needs no defense. In the clinic, however, "its application is infinitely more difficult because the subject of experiment is man. On occasion it is possible, when the procedures employed are harmless or when willing and often courageous volunteers offer themselves as subjects for experimentation. Otherwise, the clinical investigator must have recourse to animals to test his hypotheses, must go to the laboratory and become temporarily a pathologist or bacteriologist, a chemist or physiologist. That he is increasingly able to do so is all to his credit, but when he does so let him remember that he has temporarily abdicated his position as a clinical investigator, and that if clinical investigation is to profit he must return to the more difficult problems of the clinic to test out there the hypotheses that he has in turn developed during his sojourn in the laboratory."

[10] F. G. Blake, "Clinical Investigation," SCIENCE, 74: 27, July 10, 1931.

Such a professional view-point, applied to the human patient, is by no means derogatory to traditional physiological research in the laboratory. It defines the partnership of interest that all the biological sciences have in promoting the understanding of disease. It welcomes the help that they may give, while insisting quite properly that disease involves something more. As Blake concludes: "It has become more and more apparent to the clinical investigator, a fact of course long recognized in physiology through the influence of Claude Bernard, that the search for specific causes, whether they be living organisms, chemical substances, deficiencies or what not, is but one aspect of a many-sided picture and that a real comprehension of the etiology of disease resides in an understanding of all the conditions or circumstances under which it develops. Here we are concerned with pathogenesis, not etiology in the conventional usage of the word; the study of the interplay of specific agents, environmental factors, and human susceptibilities."

The great importance of physiological researches on man is obvious; but so-called "hominal" physiology should supplement rather than supplant a method of investigation that has been so fruitful in the past and surely has not yet exhausted its possibilities of discovery in relation to the promotion of human welfare. Let us be receptive, yet somewhat wary toward the criticisms of those who exhibit a lack of sympathy or understanding toward the laboratory and its conventional procedures. In any scientific field the methods of research that are most essential can as a rule be selected best not by the layman or the theorist but by persons who have actually been engaged in its development.

Appreciation of the normal processes of life represents the starting point or the foundation of medical knowledge; without this, an adequate understanding of those deviations that represent disease can not be satisfactorily acquired. Dependence upon our instincts or on chance observations that circumstances may permit in the case of man himself can help us only in occasional instances to reach the goal of medical effort. "Quite true and obvious," we hear the critic saying; and then he asks whether, after all, there is not too much of what is called "research" of all kinds, clinical as well as laboratory; whether much of it is not quite useless and even cumbersome to the practitioner.

That person must indeed be endowed with unerring judgment who can readily distinguish between scientific value and ultimately utility in research. Who shall say what the practical aspect of a scientific undertaking or its outcome may be? I recall that the

discovery of iodine in the thyroid gland by my teacher, Eugen Baumann, was the result of a chance observation in the course of an experiment—a lucky laboratory "accident," you may say. The discovery of the x-rays by Roentgen was a by-product of another research that was likewise a chance observation. These important contributions were not the outcome of planning directed to man on the one hand or industry on the other. They were the results of the unhampered undertakings of prepared minds in the laboratory.

Many years ago I heard Sir Michael Foster remark, with apparent satisfaction, that the frog and the myograph, the dog and kymograph were no longer the alpha and omega of physiology. He was referring to the growing interest in what is now called general physiology that selects its objects for study from the lowest forms of life as well as from mammals. To-day one hears complaints that our physiological journals have become memoirs of the rat and the mouse.

Is animal experimentation really decadent? Has the laboratory actually become sterile? Is its outlook unpromising? A few haphazard glimpses into its past records may help us in evaluating its place in the scheme of medical progress. Recall, for example, the story of the thyroid: the observations of Schiff and others that it is an essential structure; the discovery of iodine and its indispensability to life; the isolation of thyroxine by Kendall; the synthesis of this therapeutically potent derivative by Harrington. It required the experimental demonstration of the function and indispensability of the parathyroid structures in animals to render safe the thyroid surgery initiated by surgeons like Kocher and Halstead. These are the records of a half century of endeavor in the laboratory, beneficent beyond measure to man, yet due primarily to the possibilities of the use of animals for research.

Again, we may point to the dramatic chapters on the discovery of pancreatic diabetes and the use of insulin in medicine. They include the pioneer surgical experiments of v. Mering and Minkowski on animals; the cogent reasoning and effective laboratory technique of Banting and Best and their coworkers; the chemical ingenuity of Abel in crystallizing insulin, the invaluable pancreatic hormone. These are not merely records of a distant past. They represent sequences of the laboratory's contributions and the beneficent part played by animal experimentation until this very year; and the end is not yet. The current conceptions of hormones—products of small organs bringing about all manner of physiological adjustments—are yearly adding to the effectiveness of therapy or furnishing clues to surgery.

Some of you may have read the interesting story recently published by W. H. Park[11] of the fight against diphtheria in New York City during the past half century. Tracheotomy was supplanted by intubation, introduced by O'Dwyer in 1884. These "hominal" methods were rarely more than palliative. The discoveries of Klebs and Loeffler relating to the diphtheria bacillus; the monumental contributions of Roux and Bering in the study of immunization and the production of diphtheria antitoxin; the chemical refinement of antitoxin; the development of toxin-antitoxin for nation-wide immunization of susceptible children—these are some of the factors that have reduced the mortality of a dreaded disease endemic in our largest city for at least 150 years, from as high as 280 per hundred thousand in 1875 to 2.8 per hundred thousand in 1930. The cases have dropped from 15,000 in a much smaller population to 3,800 in the present 7,000,000. What a tribute to the value of the laboratory and its experimental animals, without which this great advance in human well-being would have been utterly impossible!

It would be a comparatively easy task to multiply such illustrations, not in defending but rather in extolling the contributions of animal experimentation. They can be found in every department of the medical sciences. A few further examples, presented in hasty review, must suffice here. Recall, if you will, that it was a physiologist, Haldane (whose brilliant researches on normal breathing had marked him as most likely to determine what was wrong), who was sent to investigate the hideous consequences of the first mysterious war gas attack in 1915. He found that want of oxygen in the gassed victims was the prime cause of the symptoms; and effective methods of relief were consequently instituted.

The management of caisson disease and the conquest of altitude, so that a height of nearly 8 miles can be reached by the modern aviator, owe their success to the dictates of physiological research begun in the laboratory. The treatment of carbon monoxide poisoning—a growing menace of modern life—has been greatly facilitated by physiological workers, notably my colleagues Henderson and Haggard at Yale University. Through exhaustive preliminary researches on animals they have demonstrated the possibilities of formerly interdicted inhalations of carbon dioxide along with oxygen in the regulation of respiration in various untoward conditions.[12]

[11] W. H. Park, "The History of Diphtheria in New York City," *Am. Jour. Dis. Child.*, 42: 1439, December, 1931.

[12] Y. Henderson, "Applications of the Physiology of Respiration to Resuscitation from Asphyxia and Drowning and to the Prevention and Treatment of Secondary Pneumonia," *Yale Jour. Biol. and Med.*, 4: 429, March, 1932.

In a volume entitled "Scientific Research and Human Welfare," the author[13] remarks:

> In the discovery of anesthetics we have another of the many cases in which patient scientific research extending over a long period of time and calling in the services of the scientists of a number of countries has come to the aid of man to bless his life and to make his abode on earth more pleasant.

One need not revert to that eventful day, October 16, 1846, when Dr. Warren, having completed the first public demonstration of the use of ether, turned to the audience in the amphitheater of the Massachusetts General Hospital and said slowly and emphatically, "Gentlemen, this is no humbug." All of you can recall that only recently an American physiologist, Dr. Luckhardt, of Chicago, has brought forth a contribution to painless surgery in his studies of ethylene.

Physiology is beginning to explain "the true inwardness" of diseases of metabolism. It is correcting some of the mistaken notions, such as that which made uric acid a bugbear in the past. The meaning of the calorie in nutrition has become established and has brought help to the physician in so-called calorie feeding in fever as well as in the management of obesity.

From the laboratory, too, have come those guiding principles that are so useful in the difficulties presented by cases of intestinal obstruction. Loss of fluid and chloride through persistent vomiting and profuse diarrhea have been established as serious manifestations that can be successfully combatted. Anhydremia has become a reality to the clinician through the tuition of the laboratory. The demonstration of the nature of nutritional edema in feeding experiments on the lowly rat has supplied cogent indications for the better management of a unique disorder with its symptom of decreased serum proteins. The newer knowledge of the genesis of the various so-called avitaminoses is too familiar to you to deserve detailed comment. May I remind you, however, that although scurvy has been a medical problem for generations

> little progress was made in our exact knowledge of the conditions giving rise to scurvy, whether in the adult or the infant, and of the best remedies, until it became possible to investigate the question in the laboratory by experiments on animals. This important advance was made in 1907 by the Norwegian investigator Axel Holst, who found that guinea-pigs developed a disease closely resembling human scurvy when fed on a diet of grain and water.[8]

[13] F. S. Harris and N. I. Butt, "Scientific Research and Human Welfare," the Macmillan Company, New York, 1924.

The newest chapter in the story will include the isolation and possible synthesis of the antiscorbutic vitamin, vitamin C. Consider what this may mean to armies and navies and polar exploration for which scurvy was an ever-menacing problem in the past.

The etiology of gastro-intestinal ulcers is not likely to be solved at the bedside alone. Significant hints are coming from the physiological laboratories in researches like those of Ivy and others. Hematology would, I suspect, make far greater progress if its chief devotees became reconciled in larger degree to the help that animal experimentation may afford. The study of the function of the bone marrow calls for something more than a few thousand blood counts and blood smears at the bedside. Barcroft's observations of spleen function in animals have done more than years of casual observation in the human clinic to throw some light on the hitherto obscure workings of a large organ intimately connected with the blood stream.

In the February issue of *Hygeia,* Kilduffe has praised the possibilities of animal experimentation regarding the chronic leukemias. He reminded his readers how fortunate it is that birds and certain mammals are subject to a similar if not identical condition, as this renders it possible to study the disease under conditions impossible in the human being. For only through such study, he adds, can it be hoped ever to discover ways and means for the cure or prevention of these peculiar "tumors of the blood."

In these days of recurrent criticisms there is an instructive significance in the findings of the widely heralded Calmette antituberculosis vaccine trials at Luebeck, Germany. The court held, according to the cabled reports,[14] that adequate tests on animals would almost certainly have averted that regrettable catastrophe.

Lest some one may charge that surgery is far less dependent than medicine upon animal experimentation let me remind you that to-day university departments of surgery are no longer organized without facilities for animal studies. A distinguished surgeon has assured me that new operative procedures are almost always tested on animals. He reminded me that the technique of intestinal sutures, of blood vessel surgery and transfusion, the modification of intracranial pressure of which neurologic surgery makes use, the development of suitable catgut and other suture materials —each of these has been a sequence of experiments on animals. One of the greatest advances in gall bladder surgery has been the introduction of the Graham test —a direct outcome of laboratory experiments on phthaleins. Who can predict the advances that might

[14] *New York Times,* Sunday, February 7, 1932.

be made if the problems of human ulcer could be studied effectively on laboratory animals?

Why multiply illustrations? Our thesis is not a denial of the great good that can come from "hominal" physiology. The "clinical physiologist" deserves encouragement. We need more persons capable of applying physiological knowledge in the study of disease and its treatment. My plea is rather that distinguished devotees of practical medicine and surgery shall refrain from unwarranted derogatory attacks upon one of the best helps of their profession in the past. It is difficult enough to fight suffering, disease and death without being obliged to fight the ignorance and prejudices of those who would tie the arms of the laboratory worker. The ultimate objective of all methods of attack upon ignorance is the same.

In closing I can not do better than to quote from the significant words of the distinguished biochemist and Nobel laureate, Sir Frederick Gowland Hopkins, president of the Royal Society of Great Britain:

> While scientific advances of every kind tend to react upon and assist medicine it is certain that without experiments upon animals the subject can not properly advance. The necessity continually arises for performing preliminary experiments upon living animals before this or that new piece of knowledge can be applied to the relief of humanity. Much of the new knowledge can, indeed, only be won by means of such experiments. The alternatives are three: ignorance and lack of progress; experiments upon human beings; or experiments upon animals. It should not be difficult to choose among them. The emotions which have led many to reject the last alternative are among those deserving the highest respect. Such emotions, however, have too often been allowed to express themselves in combination with ignorance and with an absence of all sense of proportion. . . . The experimentalist has nothing to fear, but everything to gain, from the formation of an informed and healthy public opinion concerning his work.[15]

OBITUARY

K. K. GEDROIZ

THE staff of the Department of Soil Science of the New Jersey Agricultural Experiment Station and of the College of Agriculture of Rutgers University wish to place on record in SCIENCE their keen sorrow and regret at the death of Professor K. K. Gedroiz and, with their colleagues at other institutions and in other countries, to recognize his passing as a most serious loss to science and to agriculture. The young but rapidly growing science of the soils has lost in Professor Gedroiz an outstanding scholar whose contributions to our knowledge of the base exchange capacity and the colloidal properties of the soil have revolutionized our ideas concerning this important branch of soil science. As president of the second International Soil Science Congress that convened in Russia in 1930, he contributed materially by his great reputation toward making the congress a success, even though ill health prevented him from taking a part in its deliberations. Russia has given many great men to soil science, and the name of Gedroiz will be remembered, with those of Dokutschaiev, Sibirtzev, Kossowitch, Glinka and many others, as having laid the foundation of a new science, which is at the very base of agriculture. The director and the members of the staff of the New Jersey Agricultural Experiment Station and of the College of Agriculture of Rutgers University wish to convey to the Academy of Sciences of the Union of Socialist Soviet Republics and to their colleagues in the union and in other countries this message of sympathy and profound regret.

A. W. BLAIR
SANTE MATTSON
S. A. WAKSMAN

RECENT DEATHS

DR. WILLIAM PATTEN, professor emeritus of zoology at Dartmouth College, died on October 27. He was seventy-one years old.

RUDOLPH FREDERICK SCHUCHARDT, chief electrical engineer of the Commonwealth Edison Company, Chicago, past president of the American Institute of Electrical Engineers and a member of the administration board of the American Engineers Council, died on October 26 at the age of fifty-six years.

CURTIS CLARK HOWARD, professor of toxicology at the Ohio State University for more than forty years, died on October 23. He was seventy-eight years old.

DR. ERNST HUBER, associate professor of anatomy at the Johns Hopkins Medical School, has committed suicide. He was forty years of age.

SIR EVERARD IM THURN, explorer, anthropologist and naturalist, died on October 8, at the age of eighty years. Sir Everard was formerly curator of the British Guiana Museum and in 1919–20 president of the Royal Anthropological Institute.

ALFRED CHASTON CHAPMAN, consulting research chemist, of London, England, died on October 17 in his sixty-third year.

DR. KARL E. RITTER VON GOEBEL, professor of botany in the University of Munich, and director of the Botanical Gardens, died on October 10, at the age of seventy-seven years.

MEMORIALS

A MARBLE bust of Commodore Matthew C. Perry has been presented to the Navy Department by his

[15] "Science and the Nation," edited by A. C. Seward, Cambridge University Press, 1917.

grandson, Perry Belmont, and will be placed in the projected new naval museum. It is the work of Erastus D. Palmer, of Albany.

THE *Bulletin* of the University of Maryland School of Medicine dedicated its July issue to the memory of Dr. C. Hampson Jones, late professor of hygiene and public health at the school and commissioner of health of Baltimore.

IT is planned to establish a memorial library of medicine in Tokyo in memory of the late Baron Kitasato. Count Kiyoura has been elected chairman of the committee appointed to carry out the plan.

THE London County Council has affixed a glazed-ware tablet on No. 3, Manchester Square, W., to commemorate the residence there of the eminent neurologist, John Hughlings Jackson.

THE Leiden branch of the Royal Horticultural Society of the Netherlands, in order to commemorate the founding of the acclimatization garden for Japanese plants "Nippon," by Jhr. Dr. Ph. F. von Siebold, held an exhibition from May 4 to 8, in the City Auditorium of Leiden, of living Japanese plants, shrubs and trees. Many of these are descendants of plants imported by von Siebold. Belgian and Dutch horticulturists collaborated to make this collection as complete as possible. At various other institutes of the University of Leiden, smaller exhibits were held of the ethnographical, zoological and botanical material gathered by von Siebold. Biographical materials were shown at the University Print Collection. In the University Gardens, which still contain more than forty trees and shrubs of von Siebold, a bronze statue, by the sculptor O. Wenckebach, was unveiled by his grandson and by the grandson of his head-gardener.

SCIENTIFIC EVENTS

THE PARLIAMENTARY AND PUBLIC AFFAIRS COMMITTEE OF THE BRITISH SCIENCE GUILD

THE London *Times* reports that the council of the British Science Guild plans to develop its proposals for the fostering of the scientific attitude in public affairs. Some months ago, representatives of scientific institutions and societies attended a conference, which decided to form an organization entitled to speak for science as a whole, and to act as an advisory and consultative body to members of both Houses of Parliament who are interested not only in the relation of science to industry, but in the application of the scientific spirit to all national, imperial and international affairs.

The committee already exists in embryo. The societies which it represents include the guild itself, the Institutions of Civil, Mechanical, Electrical and Heating and Ventilating Engineers, the Institute of Physics, the Institution of Naval Architects and the Royal Institute of British Architects.

The movement was originated in the lifetime of the last Parliament by Major A. G. Church, the organizing secretary of the guild, and the invitation which brought the scientific institutions together was signed by Sir Samuel Hoare, now Secretary of State for India, in his capacity as the guild's president. Major Church recently reported that he had received invaluable help in the early stages of the movement from Mr. Ormsby-Gore, now first commissioner of works, and had been much indebted for support outside Parliament to Sir Richard Gregory, the editor of *Nature*, who is the chairman of the guild's council of management.

A draft constitution for the new body had been drawn up with a program of work. The fulfilment of that program would depend on the financial support which it received. It was of the greatest importance that the body should be independent of the government, so that it should have full liberty of criticism. There was some danger that it might be mistakenly regarded as a government body if, as had been suggested, it received the title of the National Science Advisory Council. As the Parliamentary and Public Affairs Committee of the British Science Guild, the name and constitution of the organization would be more accurately suited to its function.

One of the chief duties of the new body will be to hold a watching brief, on behalf not merely of the scientific community but also of the nation, whenever governmental and other institutions discuss subjects which affect the national interests. To add impetus to its task, the British Science Guild has committed itself to the production of an ambitious volume, designed to help the British people, including its statesmen, politicians, administrators, financiers and industrialists, to realize the value of the contributions which science has already made to the nation's progress, and the potentialities of science in the evolution of a better order of society.

"We shall be as much concerned with the education of the scientific community as with that of the body politic," Major Church said. "Governments will ignore scientific workers as long as they themselves remain indifferent to the affairs of state—more indifferent, it appears, than any other section of the community. Yet statecraft is now mainly a question of making humanity fit for science, or at least of

modifying the political and economic systems of the world to enable its inhabitants to enjoy the fruits of scientific endeavor."

THE POLAR YEAR

A DISPATCH from the United Press, dated from Paris on October 2, reports that the first news has been received from the French "Polar Year" scientific mission of fifteen men stationed at Paul Doumer, Rosenvinges, on Scoresby Sound, Greenland.

The expedition will remain at the station until the ice breaks up in August, when Dr. Charcot expects to lead an expedition of two ships which will bring the party out. The government has agreed to leave the camp standing after that as a base for further missions.

The mission reported that an unusually severe winter began in September, two weeks ahead of time. Gales are blowing over Greenland and the temperature is below zero both day and night. In the camp, hastily built after landing on July 27, the men are living as comfortably as possible. They listen in, during their leisure time, to American and European radio broadcasts.

The station was completely installed by August 10 and methodic scientific observations were started on September 1. These observations include precise measurements of magnetic and electric fields, the conductibility and ionization of the atmosphere, aerological soundings, the study of atmospheric and oceanic phenomena, hydrographic and atmospheric currents and biology and geology in general.

The observations are expected to result in a great advance in knowledge of the source of North Atlantic storms, and are being made preliminary to the establishment of a string of meteorological stations which will ultimately furnish transatlantic airmen with precise information and storm warnings.

The mission reported that the sound was open to ships for less than thirteen days this year, and that soon after the polar exploration ship of Dr. Charcot and the French naval ice-crusher *Pollux* left, having landed the mission's 300 tons of equipment, the sound froze over again.

The expedition is under the command of Naval Lieutenant Habert and includes three officers, eight sailors, a doctor and two representatives of the Ministry of Public Instruction.

EUROPEAN TRIP OF ENTOMOLOGISTS

A FIFTEEN weeks' trip of unusual interest ended on September 26, when the S. S. *Minnetonka* docked at New York. Planned primarily for American entomologists wishing to attend the Fifth International Congress of Entomology in Paris during July, it afforded exceptional opportunities for scientific collecting and for sightseeing, both before and after the congress. The itinerary was planned by a joint committee of the Entomological Society of America and the American Association of Economic Entomologists, of which Dr. O. A. Johannsen, of Cornell University, was chairman, and by Dr. J. Chester Bradley, of the same institution, who acted as personal conductor of Group A. Those starting early in June were able to visit northern Germany, Denmark, Sweden and Norway before the arrival in France of Group B, led by Dr. P. W. Claassen, of Ithaca, New York. Together the groups proceeded through the Netherlands and Belgium, reaching Paris in time for the meetings of the Centennial of the French Entomological Society, and remaining through the session of the congress which immediately followed. After leaving Paris an auto trip was made through the Pyrenees mountains and across southern France to the foot of Mont Blanc, and still later Group A traveled through Italy, the Tyrol and Germany. Of especial interest to members of the party were the Agricultural Experiment Station and Museum of Folk History at Lyngby; the botanical gardens at Lund and Uppsala; the summer home of Linnaeus at Hammarby; Lake Torne-trask, near Abisko, where considerable collecting was done; the land of the midnight sun, including a cruise along the Norwegian coast from Narvik to the North Cape; the zoological gardens at Copenhagen, Hamburg, Dresden and Berlin; the islands of Volendam and Marken in the Zuider Zee; the prehistoric cave of Nieaux in the foothills of the Pyrenees, where engravings and paintings of bison, wild boar and goats were seen; the medieval walled towns of Foix, Carcassone and Avignon; the home of Jean Henri Fabre at Serignan; the source of the Rhone River at Gletsch; the journey by train and teleferique to the summit of the Zugspitze at Eibsee; the ruins of the ancient Greek temples at Paestum and the ascent of Vesuvius to the rim of its newest crater. Before sailing from Southampton members of the party visited the Rothamsted Experimental Station at Harpenden, the Zoological Museum at Tring and Oxford University.

ENTOMOLOGICAL WORK OF THE UNIVERSITY OF CALIFORNIA AT RIVERSIDE AND LOS ANGELES

THE first meeting of the year of the Southern California Entomological Club was held at Riverside on September 16. Following the reading of papers an inspection was made of the new entomology building (briefly described in SCIENCE, Vol. 76, p. 290) and the new insectary which was completed last year.

This insectary is unique in that it consists of twenty

insect-proof rooms where foreign parasitic insects, as well as others, may be studied without the hazard that undesirable parasites may escape and become established. The organization of work in entomology in the University of California was explained by H. J. Quayle, and an announcement made of the inauguration of the teaching of entomology in the University of California at Los Angeles.

Because of the diversity of crops in California and the consequent wide range of insect problems, as well as the size of the state, the entomological work in the university has, since 1914, been conducted from two centers, Berkeley and Riverside. W. B. Herms, head of the Division of Entomology and Parasitology at Berkeley and Davis, is in charge of the work in agricultural entomology in northern and central California and in charge of medical and veterinary entomology throughout the state. H. J. Quayle, head of the Division of Entomology at Riverside and Los Angeles, has general charge of the work in agricultural entomology in southern California and in so far as the work pertains to citrus and walnuts throughout the state. H. S. Smith, head of the Division of Beneficial Insect Investigations at Riverside, has general charge of this work for the entire state.

The research work in southern California is further subdivided into: spraying investigations, which is in charge of R. H. Smith; walnut and deciduous fruit insect investigations, which is in charge of A. M. Boyce, and the taxonomic work and collection which is in charge of P. H. Timberlake.

The teaching of entomology will be inaugurated at the University of California at Los Angeles beginning in the second semester of the present year. At that time a course in general entomology will be given, which will correspond to Course I as given at Berkeley. Beginning the second semester of the following year an advanced course in subtropical fruit insects will also be offered. The undergraduate teaching work at Los Angeles will be directly in charge of A. M. Boyce. Three rooms, consisting of a large laboratory, a research laboratory and an office in one of the new buildings at Los Angeles, will be utilized for this work. Graduate work in subtropical fruit insects and beneficial insect investigations will be given at Riverside as heretofore.

SCIENTIFIC NOTES AND NEWS

THE Nobel prize in medicine for 1932 has been awarded in equal parts to Sir Charles Scott Sherrington, Waynflete professor of physiology at the University of Oxford, and to professor Edgar Douglas Adrian, Foulerton professor of the Royal Society and fellow of Trinity College, Cambridge.

THE title of Knight Commander of the Crown of Italy has been conferred on Dr. William J. Mayo and on Dr. Charles H. Mayo by the King of Italy, in recognition of their services to science and to humanity, and more especially in recognition of their kindness to Italian graduate students, studying at the Mayo clinic, and to patients of Italian origin who are cared for there. The king was represented by Consul Cavaliere A. Castigliano at a ceremony held on October 22. The professional and non-professional members of the staff and other citizens attended.

DR. CHARLES RUSS RICHARDS, president of Lehigh University, and Bruce Rogers, type and book designer, of London, graduates in the class of 1890, were given honorary degrees at Purdue University on October 15, at a special convocation arranged for this purpose at the annual homecoming of Purdue graduates. Dr. Richards was granted the degree of doctor of engineering and Dr. Rogers the degree of doctor of humane letters.

THE John Fritz Gold Medal, highest of American engineering honors, has been awarded for 1933 to Daniel Cowan Jackling, of San Francisco, for "notable industrial achievement in initiating mass production of copper from low-grade ores, through the application of engineering principles." The award was made by a board of sixteen representatives of the four national societies of Civil, Mining and Metallurgical, Mechanical and Electrical engineers.

DR. ROBERT A. MILLIKAN was presented with the distinguished service medal of the Roosevelt Memorial Association at a dinner given at Roosevelt House, New York City, on October 27. James R. Garfield, Secretary of the Interior in the cabinet of President Roosevelt and president of the association, made the presentation. The citation read: "The Roosevelt medal for distinguished service has been awarded this year in only one domain, the field of science. For this medal, I have the honor to present the name of a scholar, a teacher, a mentor of scholars, a master of research, a scientist, imaginative and pertinacious, who has explored both the infinitely vast and the infinitesimally minute, returning from sidereal space with the secret of the cosmic ray, from the crashing of worlds within the molecule with the secret of the electron's speed, a prophet of the new time, bearing to bewildered man, alike from atom and from star, news of the presence and the goodness of God."

THE Perkin Medal for 1933 has been awarded to George Oenslager for his contributions to rubber technology. *Industrial and Engineering Chemistry,* in announcing the award, says: "Mr. Oenslager has been connected for many years with the B. F. Goodrich Company and its immediate predecessors and, but for the earlier policies opposed to publicity, his work would long ago have been recognized more generally as of vast importance and directly responsible for two of the five major achievements which mark the changes that have taken place in rubber technology during the past thirty years. These five achievements may be named as reclaimed rubber, the cord tire, the carbon black tread, the nitrogenous organic accelerator and antioxidants. That one man should have played such an important part in the discovery and introduction of two of these advances is worthy of note."

J. A. FLEMING, acting director of the Department of Terrestrial Magnetism of the Carnegie Institution of Washington and general secretary of the American Geophysical Union, has been elected an honorary and corresponding member of the State Russian Geographical Society in appreciation of his services in developing the geophysical sciences.

DR. E. O. ESSIG, professor of entomology in the College of Agriculture of the University of California, has been decorated by the French government with the title of Chevalier du Mérite agricole.

ON October 7 Sir Philip Magnus, Bt., celebrated the ninetieth anniversary of his birth. He was member of Parliament for the University of London from 1906 to 1922, and in 1920, in recognition of his services to medicine in Parliament, he was made an honorary member of the British Medical Association.

FOREIGN surgeons who attended the annual clinical congress of the American College of Surgeons, which opened at St. Louis on October 17, included Sir William I. de Courcy Wheeler, of Dublin; Sir Wilfred Thomason Grenfell, of London and Labrador; Sir George Lenthal Cheatle, of London, and Dr. Jose Goyanes, of Madrid.

PROFESSOR ALFRED FOWLER and Sir Clement D. M. Hindley have been appointed members of the Advisory Council to the Committee of the Privy Council for Scientific and Industrial Research in place of Sir J. Alfred Ewing and Sir David Milne-Watson, who have retired on completion of their terms of office. Brigadier-General Sir Harold B. Hartley has been appointed chairman of the Fuel Research Board and N. V. Sidgwick chairman of the Chemistry Research Board, in place of the late Sir Richard Threlfall.

DR. AUGUSTUS TROWBRIDGE, dean of the Graduate School of Princeton University, has been granted leave of absence for the first term of the academic year. In his absence the graduate school will be managed by a faculty committee of which Dr. Robert Kilburn Root, professor of English, is chairman.

DR. OSWALD VEBLEN, Henry Burchard Fine professor of mathematics at Princeton University, who, as previously announced, will join the staff of the Institute of Advanced Study at Princeton, has presented his resignation to the trustees. Dr. Veblen has been connected with Princeton University for twenty-seven years.

DR. LYMAN L. DAINES, professor of pathology and bacteriology at the University of Utah School of Medicine, has been appointed dean of the school, to succeed Dr. Beryl I. Burns, who resigned to become head of the department of anatomy at the newly organized Louisiana State University Medical Center, New Orleans.

DR. H. A. SWENSON has been promoted to an assistant professorship in the department of psychology in the Division of Biological Sciences of the University of Chicago.

DR. OLIVER L. FASSIG and Dr. Herbert H. Kimball, both long associated with the U. S. Weather Bureau at Washington, have been appointed research associates of the Blue Hill Observatory of Harvard University.

DR. C. S. MUDGE, of the dairy industry division of the University of California, has been granted six months' leave of absence, beginning at the end of December. He plans to study in the laboratories of the Western Pennsylvania Hospital of the Institute of Pathology at Pittsburgh.

DR. R. R. STEWART, for twenty years professor of biology in Gordon College, Rawalpindi, India, has brought to the New York Botanical Garden a large general collection of plants from the northwest Himalaya and the Punjab and expects to spend the year in naming them. During May and June, he was at the Royal Botanic Gardens at Kew, engaged in the study of ferns and grasses. Professor Stewart has spent most of his summer vacations collecting in Kashmir.

DR. R. E. ROSE, director of the Technical Laboratory of the E. I. du Pont de Nemours and Company, Incorporated, was one of the guest speakers at the meeting of the Laundryowners National Association of the United States and Canada, which met in Toronto from October 17 to 20.

THE first meeting of the De Paul Chemistry and Physics Journal Society for this year was held on October 16, at the Medinah Athletic Club, Chicago.

Professor Philip Fox, director of the Adler Planetarium, was guest of honor and speaker of the evening, choosing for his discussion the recent solar eclipse.

THE first Sigma Xi lecture of the year at the University of Missouri was presented on October 25 by Dr. Bradley M. Patten, associate professor of embryology and histology, Western Reserve University School of Medicine. His subject was "First Heart Beats and Beginning Circulation in Living Embryos." The lecture was illustrated with micro-moving pictures of living chick and wren embryos.

PROFESSOR JULIAN HUXLEY, formerly professor of zoology and now honorary lecturer at Kings College, London, lectured at the University of California at Los Angeles on October 25. The title of his lecture was "The Uniqueness of Man."

THE Thomas Hawksley Lecture of the Institution of Mechanical Engineers was delivered by Lord Rutherford on November 4 on "Atomic Projectiles and their Applications."

AN Institute of Ornithology has been established at the University of Oxford. Its object is to carry out on a larger scale the work in ornithology which was started some years ago. The institute will be financed by the Ministry of Agriculture and the Empire Marketing Board. The University of Oxford will have control of this institute, for which the necessary funds are being obtained from the British Trust for Ornithology. The institute is established in the first instance for a period of five years under the direction of Mr. W. B. Alexander, working in the department of zoology and comparative anatomy.

Nature reports that H. J. Page has been appointed controller of the Agricultural Research Station of Imperial Chemical Industries, Ltd., at Jealott's Hill, Bracknell, Berks, following the release of Sir Frederick Keeble from his executive and routine duties at that station. Mr. Page was until 1927 head of the chemical department and chief chemist at the Rothamsted Experimental Station, and since that time has held the position of head of the research laboratories and chief chemist at the station of which he has now taken charge.

EIGHT engineers have been appointed to advisory membership in the Council Committee of the College of Engineering of New York University, with the idea of closely integrating professional experience and engineering training. Arthur S. Tuttle is chairman of the committee. Those appointed to the advisory committee are: Leon P. Alford, vice-president of the Ronald Press, New York; William L. Batt, president S. K. F. Industries, Inc.; Robert W. Boyd, engineer for the Turner Construction Company; John V. N. Dorr, president of the Dorr Company; George W. Fuller, specialist in water supply and sewage treatment; Frank B. Jewett, vice-president of the American Telephone and Telegraph Company and president of the Bell Laboratories; Grover Loening, president of the Loening Aircraft Corporation, and Robert Ridgway, chief engineer of the Board of Transportation, New York City.

THE Weather Bureau, which has been cooperating with Dr. R. A. Millikan in his investigations of cosmic rays as a part of the program of the International Polar Year, reports, according to the *U. S. Official Record,* that in spite of difficulties due to high winds, a large sounding balloon carrying an electroscope and other instruments was successfully launched at Ellendale, North Dakota, on September 17. The instruments have not yet been found. Dr. Millikan's colleague, Dr. I. S. Bowen, released two similar balloons at Dallas, Texas, on September 28 and 29, in cooperation with the bureau's airport station at Dallas. The instruments sent up on September 28 were found 25 miles northeast of Dallas, and preliminary calculations showed that they reached a height of about ten miles. A third balloon was released at Dallas on October 5. This work completes Dr. Millikan's balloon observations as arranged for in cooperation with the bureau. The bureau is forwarding to Dr. Millikan the data yielded by the instruments as they are found.

SIR CHARLES MCLEOD, chairman, and Lord Queenborough, honorable treasurer, have made the following appeal on behalf of the Ross Institute, London. "In 1923 a movement was started to found an institute to perpetuate for all time the name of Sir Ronald Ross, to carry on research work, and to stimulate malaria control measures in the empire. The Ross Institute was officially opened in 1926 by H.R.H. the Prince of Wales, and Sir Ronald Ross was the director-in-chief until his death. What the institute has already achieved is well known the world over, but if its work is to be continued more financial support must be forthcoming immediately. There is no endowment fund, and for two years contributions have been 25 per cent. below expenditure. This state of things can not go on much longer. Surely an effort can be made to save the institute and place it on a sound financial basis."

THE committee on scientific research of the American Medical Association invites applications for grants of money to aid in research on problems bearing more or less directly on clinical medicine. Preference is given to requests for moderate amounts to meet specific needs. Application forms may be obtained from the committee at 535 North Dearborn Street, Chicago, Illinois.

AN award of the Harrison Prize will be made, according to *Nature,* in December by a committee consisting of the presidents of the British Chemical Society, the Institute of Chemistry, the Society of Chemical Industry and the Pharmaceutical Society. The prize is of the value of about £150 and is awarded to the chemist who, in the opinion of the selection committee, during the last five years has conducted the most meritorious original investigations in any branch of pure and applied chemistry and has published his results. Further information can be obtained from the President, The Chemical Society, Burlington House, Piccadilly, London, W.1.

A CANCER research institute has been established in Tokyo, in the Imperial University Medical Department. The institute is to have a research department and a hospital, and Professor Nagayo of the university is to be the director. After 1933, the government will bear a part of the expense.

THE Forest Products Laboratory of the Forest Service, which has been maintained since 1910 in cooperation with the University of Wisconsin, has moved into its new building located west of the university campus. The laboratory for 20 years has been operating in four buildings and has several minor structures. The new building is U-shaped in plan, with five stories, a ground floor, and a penthouse over the central span between the wings. The first floor is stepped back from the ground floor, and the second, third and fourth floors are stepped back as a unit from the first. A variety of woods, including Douglas fir, ponderosa and southern yellow pine, walnut, oak, chestnut, birch and red gum, have been used in the scheme of interior finish. Facilities of the new laboratory building include a log storage yard, a sawmill, dry kilns, woodworking plant, gluing and paint shops, a mechanical testing laboratory, a creosoting plant, a wood distillation plant, a complete experimental pulp and paper mill, and several chemical laboratories.

ACCORDING to the report of the Forest Service the total receipts of the national forests for the fiscal year which ended last June 30 were less than half the total for the preceding fiscal year. These receipts —derived from timber sales, grazing fees, forest-products sales, rentals for water power, permits for hotels, summer homes and resorts and penalties for trespass —amounted to $2,294,247, as compared with $4,993,320 for 1931 and $6,751,553 for 1930. Water-power rentals were the only large source of receipts which were greater in 1932 than in 1931. Twenty-five per cent. of the national-forest receipts annually goes to the states in which the forests are located, for *pro rata* payments to their counties for the county road and school funds, and the decline in receipts will be reflected in smaller payments to the states.

DISCUSSION

FURTHER NOTES ON TWISTED TREES

I HAVE followed with much interest the discussions in SCIENCE[1] on twisted trees. These brief reports led me to make rather extensive observations in the forests of Louisiana, which afford excellent opportunity for the studies.

The observations I am reporting were made at several points in an area of pine forest about thirty miles across, most of which was in the recently named Kisatchie Wold section. The terrain was rather sharply rolling, but at no point were the trees particularly exposed to hard winds, and on every side the same type of growth extended for miles. The trees in this area were largely the long-leaf pine (*Pinus palustris*).

My first interest was to see how the relative numbers of straight-grained trees and right- or left-hand twists of this region compared with the counts reported from other sections of the country. In the above-mentioned area 1,527 trees were counted. Of this number 364 (23 per cent.) were straight-grained, 811 (53 per cent.) showed a right-hand twist and 352 (24 per cent.) showed left-hand twisting. The proportion of straight-grained trees compares very favorably with the figures presented by Wentworth[2] and Cahn,[3] but the number of trees showing left-hand twists in the area I studied is from more than

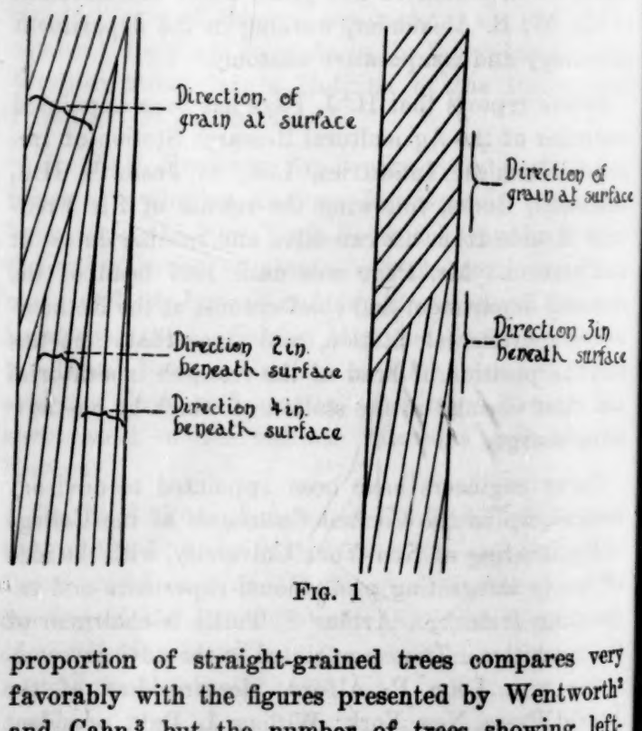

FIG. 1

[1] February 13, 1931; March 27, 1931; May 22, 1931; January 29, 1932.

[2] SCIENCE, February 13, 1931.

[3] SCIENCE, May 22, 1931.

two to eight times greater than reported by other workers.

Since many of the trees observed were fallen, weathered and partly burned, the grain in the limbs could not be determined in every case; but out of 215 observed in particular, the limbs showed the same direction of grain as in the trunk, except four cases in which the limbs showed twisting and the trunks were straight.

A new road runs through the area studied; from the roadway many trees, of various sizes, had been pulled. This condition afforded opportunity to study the roots, and the roots of 57 trees were studied. Of these, 31 (55 per cent.) showed twisting to the right of the tap root or smaller roots. Only 7 (12 per cent.) showed left-hand twisting, and 19 (33 per cent.) were straight. In practically all cases the trees had been cut so close to the ground that the direction of grain in the trunk could not be determined.

The degree of twisting varied considerably, as has been described in other regions. As measured at the surface, the direction of grain was seen, in many cases, to run at an angle of 45° to the main axis of the log. This extreme degree of twisting was observed in trees twisting to the left as well as those twisting to the right.

The most striking thing found in this study was that in any single tree the degree of twisting at the surface may be considerably greater than at any level nearer the center of the trunk or limbs. The accompanying figures illustrate conditions in trunks of actual trees and may be taken as typical examples of what was found after many careful examinations. In large, as well as small trees, this differential twisting may be taken as the general rule. This would seem to indicate that trees tend to become more twisted at the surface as they grow older. That the outer layers are twisted more than the inner ones is consistent with the observation of Cahn that larger trees were twisted more than smaller ones.

Many deciduous trees were observed that were twisted, and in some cases they were very sharply twisted, even in the limbs. Accurate records were not kept of the relative numbers, but there was a marked impression that left-hand twisting was more common than among the pines.

The purpose of this paper, simply, is to give a few additional facts on this general subject. I do not propose an explanation of the cause of twisting in trees, but I do believe that some of the observations listed here raise serious objections to the conclusion that tree twist is caused by prevailing winds. If prevailing winds cause the limbs of trees to twist, it seems reasonable to expect that the limbs on one side of a tree would twist in one direction and those on the opposite side twist in the opposite direction. All the limbs of any one tree, however, always twisted in the same direction It is believed, also, that wind could not cause roots to twist. The fact that the outer layers of the trunk and limbs are usually more sharply twisted than successive layers nearer the center is regarded as further evidence that wind is not responsible for the twisting.

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THE STINGING EPYRIS

WHEN the senior author wrote the short article, "A Small Insect Which Stings Severely," which appeared in SCIENCE for February 26, 1932 (pp. 243–245), he was unaware of the fact that the stinging propensities of the very same insect—*Epyris californicus* (Ashmead)—had previously been reported in SCIENCE by a physician, Chas. E. von Geldern, M.D.,[1] of Sacramento, California. In his article are described fully the systemic disturbances following the sting of the tiny insect from the medical view-point. Fortunately, the family referred to as living at Clarksburg is the same in both articles. In view of the increasing interest in the insect it was deemed desirable to ascertain more fully the present status of the effect of the stings on the various members of the family in question. Accordingly, the junior author, who happens to be conducting entomological investigations in the same region and who has become acquainted with the different members of the family, has secured the additional facts presented herein. The family is now composed of father, mother and four children, aged 13, 11, 9, and 3, respectively. The three older children only are mentioned in Dr. von Geldern's observations. Whereas in 1927 the father and mother both suffered considerable discomfort following the sting of the insect which resulted in asthma, numbness, nausea, localized itching and cramps, and diarrhoea, they are no longer affected seriously. For the past two years the stings have caused neither abdominal pains nor nausea. At that time also the third child, then 4, and the first, then 8, were no longer subject to manifestations of discomfort, while the second son, then 6, was greatly disturbed. At this writing the fourth boy is only irritated by the stings. The third, who up to a short time previously was only irritated, when last stung became flushed and very weak. The second son, when first stung, exhibited symptoms of asthma and general discomfort, but apparently became more or less immune until early in March, when a sting caused a flushed and swollen face and a burning of

[1] "Systemic Effects Following the Sting of a Species of *Epyris*," SCIENCE, 65: 1682, March 25, 1927, pp. 302–303.

the eyes. The oldest son is no longer bothered, except a local irritation at the time of the stinging. On April 9 he was stung in several places on the back which caused severe irritation, but no systemic complications followed.

In the experience of this particular family, over a space of nearly ten years, the very young children appeared to be only slightly affected by the stings of *Epyris*. As they grew older there was a period, from 5 to 10 years of age, when systemic complications arose, followed by a marked decrease in these symptoms.

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MUCIFICATION OF THE VAGINAL EPITHELIUM OF MICE AS A TEST FOR PREGNANCY-MAINTAINING POTENCY OF EXTRACT OF CORPORA LUTEA

IN August, 1931, we set forth in SCIENCE[1] the possibility of the use of histological changes in the vaginal mucosa of mice as a practical test for potency of extract of corpora lutea. This suggestion was based upon the fact that "Histological changes of the vaginal mucosa, comparable to those occurring during pregnancy, were found when normal, adult, unmated female mice were treated, just after oestrus, with an extract of corpora lutea, . . . with daily injections of extracts for periods ranging from 3 to 14 days." The histological changes referred to consisted of a mucification of the vaginal epithelium giving a "picture characteristic of pregnancy."

This view, however, was disputed by R. K. Meyer and W. M. Allen this year in SCIENCE[2] as follows: "The production of vaginal mucification by corpus luteum extracts which maintain pregnancy in ovariectomized pregnant animals, as described in a recent article in SCIENCE by Harris and Newman, is, we believe, not a test for progestin but a test for the small amount of oestrin which the extracts used by them undoubtedly contain."

The position taken by Meyer and Allen was based upon the fact that they were able to produce mucification "in one adult guinea-pig, new-born guinea-pigs, mice, and rats with Parke, Davis and Company's theelin (crystalline oestrogenic preparation from the urine of pregnant women)."

It should be noted that while Meyer's and Allen's results are of considerable interest, they scarcely seem to justify, *a priori*, the application which these experimenters made of them to our results, inasmuch as Meyer and Allen state that, "The method we have used in general is to castrate adult rats, mice, and guinea pigs," while we[3] definitely specified the use of "normal" mice

The practicability of any biological assay depends, of course, upon careful adherence to the described method in respect to all variables. Certainly, in the present instance, the presence or absence of ovaries in the test-animals might well be considered a variable of the greatest importance.

In actual tests, such seems to be the case. While we do not question, in any respect, the facts of Meyer's and Allen's results, we do find that when we use "normal," *i.e.*, not ovariectomized, mice we are unable to produce vaginal mucification typical of pregnancy by daily injections of Parke, Davis and Company's theelin. In these tests (14 animals) we used doses ranging in individual cases from 0.05 r.u. per day for 8 days (the optimum dosage for the production of mucification in ovariectomized mice, according to Meyer and Allen) to 0.5 r.u. per day. Save for the fact that we used normal mice in all cases, whereas the workers cited used ovariectomized animals, the variables, as far as we can judge, were under as similar control as could be expected in two different laboratories.

Thus, from our work it appears that the injection of an oestrin preparation into otherwise normal mice does not bring on mucification of the vaginal epithelium.

As a result of this work, we are inclined to deny the implication of Meyer and Allen in respect to our previous publication.[1] Though one may still maintain that the corpus luteum "hormone" in our extract so conditions the test-animals that it permits "the small amount of oestrin which the extracts . . . undoubtedly contain" to have the same reaction as it would on an ovariectomized animal, the important fact for the moment is that the extract is a crucial factor in the reaction, and that our test as described[1] still seems to be practical for the purpose originally set forth.

It is, perhaps, timely to recall that the end results of many biological assays are often producible by wholly different substances, the end result being of test-significance only when variables are controlled as indicated, and oftentimes even then only when the experimenter has a fairly good notion of what substance he is testing.

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[1] Reginald G. Harris and Dorothy M. Newman, "A Practical Test for Potency of Extract of Corpora Lutea," SCIENCE, 74: 182, 1931.

[2] Roland K. Meyer and Willard M. Allen, "The Production of Mucification of the Vaginal Epithelium of Rodents by the Oestrus Hormone," SCIENCE, 75: 111, 1932.

[3] With the technical assistance of Dorothy M. Newman.

SUPPLEMENT TO THE NOTE ON NECROBIOTIC RAYS[1]

IN his note on necrobiotic rays, due to the lack of space, the writer failed to express his thanks to the institutions and scientific men who were of assistance to him in his experiments, postponing these thanks until the appearance of his full paper. In view of the fact that this paper may not appear for a long time, the writer wishes to express his thanks at this time to the persons concerned.

The experiments on necrobiotic rays were begun at the Desert Sanatorium (Tucson, Arizona, in January, 1931), continued for about two months in the laboratory of the Biological Department of the California Institute of Technology (Pasadena, California), and then in the laboratories of the University of California (Berkeley, California), where they first succeeded. Accordingly, the writer wishes to express his thanks to Dr. Pinner and Dr. Davis, of the Desert Sanatorium, for their interest in his work and their valuable advice, to Dr. T. H. Morgan, of the California Institute of Technology, for making it possible for the writer to continue the experiments in the laboratory of the institute, to Professor Zaikovsky and Dr. Strong, of the same institute, for their interest in the writer's experiments, and their advice and help in carrying out these experiments, to Dr. Holman, of the department of botany of the University of California, for furnishing a dark room for the experiments, and to Dr. White, of the Department of Physics of the same university, for his advice and assistance.

The writer wishes to express his especial thanks to Professor V. M. Zaikovsky for his outstanding interest in the experiments on necrobiotic rays. It was he who drew the writer's attention to the possibility of an explanation of the protective effect of ultra-violet rays on protoplasm by a synthetical process which they may produce in the cell. He also suggested, after the failure of the writer to prove the presence of the rays by means of dry photographic plates, that the writer should use silver bromide emulsions for the same purpose. According to his order, the quartz tubes initially used in the experiments were made for the writer. He also constructed a special apparatus to photograph the rays. Professor Zaikovsky's advice was found to be very useful in the writer's experiments at the University of California, where the rays were first observed.

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SOME HUMAN EYE-SPOTS CLASSIFIED ZOOLOGICALLY

THIS note might have some slight interest to oculists and to entomologists. During the last few weeks my eyes have become very dim and I can no longer read. Awaiting the time for an operation, I have been interesting myself by watching my eye-spots—those fragile things that float before one's eyes, apparently in space. I have recognized three species of insects, two plainly, and the third rather dimly. The first would be *Pelecinus polyturator,* except for the fact that it has spotted wings and apparently the venation of a trypetid fly. Were it really an insect, I would call it *Pelecinoidea* (new genus) *trypetoidea* (new species). The second is the pupa of *Culex pipiens.* It has a very long abdomen and I can not see the anal flaps. But I can see the respiratory trumpets on the thorax and it is plainly Culicine—not Anopheline. Of the third I am not so sure. It looks like one of those curious parasites of ants that belongs near Orasema, species of which are so beautifully figured by Peter Cameron in the "Biologia Centrali-Americana," and by Wheeler in his well-known book on ants.

Other biologists who have misused their eyes (as I have) may amuse themselves by classifying their eye-spots. The entomologist should have no trouble. Perhaps the botanist can do something of the sort. The herpetologist should have no trouble. The bacteriologist will have difficulty for lack of culture media. The nematologist should, I think, be able to do a lot of imaginary work, but I can't imagine that the chemist or the mathematician can use this method of passing the time away.

L. O. HOWARD

WASHINGTON, D. C.
October 19, 1932

SCIENTIFIC BOOKS

Studies on the Variation, Distribution and Evolution of the Genus Partula. III. The Species Inhabiting Moorea. By HENRY EDWARD CRAMPTON. Carnegie Institution of Washington, Publication 410, 1932.

IT is well known that it was the existence of closely related but distinct species in the different islands of the Galapagos Group that first convinced Charles Darwin in 1835 that such species must have arisen by descent with modification from common ancestral species. Ever since that time the fauna and flora of oceanic islands have been favorite objects of investigation with students of organic evolution. The extraordinary interest which has been shown by naturalists

[1] SCIENCE, August 19, 1932.

in the extremely varied forms of land snails of the Pacific Islands has its origin in the fact that here one comes into close contact with evolution as it is occurring in nature in restricted and isolated areas. Many of these islands have their own peculiar species of snails and even adjoining valleys on the same island may have distinct but related species and varieties. Many naturalists have realized that an intensive study of these narrowly localized species and varieties might be expected to throw much light upon the methods and causes of organic evolution as it is taking place in nature.

Professor Crampton undertook an extensive and intensive study of the genus Partula, one of the most variable of these land snails, more than twenty-five years ago. Working under the auspices of the Carnegie Institution of Washington, he has made many journeys to the widely scattered islands of the Pacific and has collected hundreds of thousands of snails of this genus, noting in particular the exact geographical and ecological situation of each species and variety and making a most detailed biometrical study of their shells. The results of this work have appeared in three volumes, the first of which was issued in 1917 and dealt with the species of Partula inhabiting Tahiti; the second, published in 1925, with the species on Guam and Seipan, the third, recently issued, with the species inhabiting Moorea. Altogether this series probably represents the most extensive and monumental work ever published on a single genus of invertebrate animals. The first volume contains 311 pages of letter press, 252 statistical tables and 34 plates; the second, 116 pages, 62 tables and 14 plates; the third volume, 335 pages, 156 tables and 24 plates—a total of 762 pages, 470 tables and 72 plates, 32 of which are colored lithographs of nearly 1500 shells—and all devoted to a single genus of pulmonate gasteropods.

The author states that this third volume of the series goes farther than the previous ones and the results are more numerous and more definite. Especial efforts have been made to evaluate the environmental and genetical factor in evolution and the conclusion is reached that environment has little if any effect,—a conclusion which is contrary to the opinions of many previous students of this group. In explanation of the aims of his work and its relation to experimental studies of evolution, he says (p. 191): "The present study deals with species and varieties in a state of nature and with the differences displayed by the snails down to the unitary items of individual diversity. Its category, therefore, is sharply contrasted with that of experimental studies in the laboratory and garden, although the two have the common element of an interest in the initial episodes of organic differentiation. The results of my own studies accord fully with those of experimental genetics, as I understand them to be capable of formulation in the above-stated terms." Nevertheless it is unfortunate, as the author himself acknowledges, that he has not been able to apply experimental breeding to the analysis of these many so-called varieties and mutations. Until this is done, conclusions as to their origin and relationships must remain largely hypothetical. From the standpoint of a complete study of this genus it is also unfortunate that the only characters of these snails that are dealt with are those of the shells, although when one considers the extent of the biometrical tables needed to analyze these, one shrinks from the thought of what would be necessary to deal with all the organ-systems in this manner.

Only the most general summary of the principal results of this work can be mentioned in this review. The occasional appearance of sinistral forms in dextral species, or the reverse, has received careful attention. In some instances both dextral and sinistral young are borne by the same parent and the author concludes that the cause of this reversal of the usual asymmetry is genetical, which accords with the findings of Boycott, Diver, Garstang and Turner on certain species of Limnaea, where mendelian segregation does not occur until the third filial generation, instead of the second, as is usually the case.

The author finds no evidence in favor of orthogenesis, although he does find that there is a direct correlation between the degree of likeness of different forms and the geographical proximity of their habitats. Furthermore, each species has its own characteristic degree of variability. "The evidences are cumulative," he says (p. 194), "without any discrepancy, that so far as the present material is concerned the factors responsible for specific, varietal and lesser distinctions are congenital in nature and location (*sic*) and that environmental circumstances produce no discernible effects upon the course of organic differentiation." However, he acknowledges elsewhere (p. 187) the influence of natural selection in directing the course of evolution, although, in common with most modern authorities, he denies its power to originate variations and he doubts that the individual diversities he has observed have survival value.

The manner of distribution of related but distinct species of Partula in the Society, Cook and Austral Islands leads the author to the conclusion that "an earlier land-mass extended all the way to the extreme borders of Oceania, that subsidence has led to the

segregation of one coulisse after another, and that these separated ranges subsided later to greater degrees. Some of the peaks have remained above the surface as the present 'high' islands, while others were more completely submerged to serve as the bases for the growth of corals and corallines."

Finally he states that so far as the distribution of the species and varieties of this genus throughout the island of Moorea is concerned, "the only tangible conclusion is that it is completely accounted for by local differentiation among the members of ancient stocks, more or less disseminated by their own unaided movements."

In the Galleria Antica e Moderna in Florence there is a tapestry representing God giving Adam supremacy over the animals, and the long winding procession of all animals known to the artist, which is passing before Adam, is led by a land snail. This artistic conception should form the frontispiece of any future volume which Professor Crampton may publish on the genus Partula, as indicating the important place occupied by this humble animal in the procession of the living.

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Morphologische Gesetzmässigkeiten der Evolution. By PROFESSOR DR. A. N. SEWERTZOFF. Gustav Fischer, Jena, 1931. xv, 372 pp., 21 diagrams, 131 figures. Gr. 8vo.

PROFESSOR SEWERTZOFF, in this work, brings to culmination the chief results of over forty years of study of the embryology and comparative anatomy of the vertebrates. It is, however, the immediate product of the new "Laboratory for Evolutionary Morphology of the Academy of Science of the U. S. S. R." where the author and his colleagues now continue their investigations.

The discussion centers about the evolutionary history of the lower vertebrates. An attempt is made to develop the course of phylogeny of the main groups from the facts of embryology, paleontology and comparative anatomy and with the aid of schematized, hypothetical "primitive" forms built up by combining the most general characters of existing types. Remarks are made concerning the morphological methods of phylogenetic investigation and monophyletic theory of evolution. Some of the author's previously published concepts—branchiomery, the theory of the roofing bones of the skull, the theory of the articulation of the lower jaws with the neurocranium—are elaborated. Also one notices some changes in the classification of the ganoid fishes and a criticism of Stensiö's views on the relationships of the Ostracoderms to the two modern groups of Cyclostomes. This first part of the work is intended as a basis for the subsequent section dealing with a chain of related morphological theories.

In this second part the author is concerned more with the courses than the causes of evolution. He seeks the cause of organic change in the changes of the environment and inclines to the Darwinian explanation without definitely committing himself. Believing that the whole course of evolution is an adaptive process he deals principally with structural adaptations—attempting to gain insight into the ways in which these manifest themselves, their various categories, their manner of origin in the embryo and their behavior in regressive or degenerative forms.

He seeks to develop what he calls the morphological laws of phylogenetic development, adopting a rigid system of classification of adaptations, structures and embryological processes together with elaborate definitions, and a brand new set of terms. He finds it desirable, for example, to segregate organs into two classes—those which are directly influenced by the environment and those which are not so influenced. Changes induced in the former may secondarily influence certain of the latter, these in turn may affect others functionally or topographically united to them. Upon this foundation are erected two general theories: (1) the morphobiological theory of the course of evolution, in which the general and special laws of phylogenesis are set forth, and (2) the theory of phylembryogenesis, which considers the time element in the development of phyletic changes in ontogeny.

It is believed that evolution "can only follow two chief directions—progressive (struggle for existence) and recessive (extinction)." The one is characterized by increase in number of individuals, increase in range of groups owing to crowding and subdivision of the larger groups into greater number of subgroups. The other path leads to smaller numbers, diminished range and reduction in subgroups.

It is further stated that four general methods of progressive evolution exist: (1) Morpho-physiological progression or altering of the entire construction of the form with general increased intensity of active functioning as in a bird compared with a reptile; (2) special adaptation of organs involving no general bodily change; (3) embryological change without change of adult structure, leading to increased capacity of the young to survive; (4) general morpho-physiological degradation in which some "passive organs" (*i.e.*, reproductive system) develop progressively and active organs are reduced.

There are again set down two groups of phylogenetic changes: (1) in which the function of the evolving organ is only quantitatively changed and

(2) in which a qualitative change takes place. In degeneration there may be "rudimentation" when the structure is not of use to the embryo and starts to disappear at the beginning of ontogeny, and "aphanisis," in which the structure develops normally in the embryo and disappears in the adult. Interesting examples of these categories are given, one being the dorsal vertebral musculature of the turtles, which develops to a certain period in the embryo and is later carried completely away, apparently by phagocytosis.

Again it is said that coordinations between organs or groups of organs which are changing in the course of phylogeny may be placed into two groups: (1) Morpho-physiological coordinations, in which each member of a network of parts is functionally necessary to the other, and (2) topographic coordinations, in which the organs are not united functionally. To the first group belong, for example, the central nervous system, the motor system and the skeletal muscles; to the second the brain, the roofing bones of the skull and the chondrocranium, all of which may change together owing to proximity.

Differing rates of development of various coordinated parts in the embryo lead to profound results in phylogeny. This brings the author to his theory of phylembryogenesis, which seeks to explain how and in what periods of embryonic life the changes come about that lead up to alterations in the organism. "It is usually considered that the phyletic changes begin with small, heritable variations (mutations). Our investigations bring us to the viewpoint of Fritz Muller that the phylogenetic changes in the developed organs are led up to through an alteration of the course of embryonic development of these organs.

The various modes of alteration of the ontogeny are: (1) new characters appearing at the end of ontogenesis (anaboly), in which case a true recapitulation or repetition is preserved, (2) a deviation at some intermediate stage in ontogeny resulting in recapitulation only of the earlier stages of the history, and (3) changes in the first period of ontology (archallaxis), where no traces of recapitulation can remain. A change in the tempo or rate of development of various parts gives acceleration or retardation. Such an effect can not be gained by "deviation" or "archallaxis."

Finally, it is noted that archallaxis is a method of development of entirely new structures, of rapid replacement of old organs and of rapid adaptation to new or rapidly changing environments. Anaboly is a method of accumulating small heritable variations, resulting perhaps in many diverse adaptations or in adaptations to slow changes of environment. Deviation is a process intermediate between these two extremes.

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SCIENTIFIC MEETINGS

THE COPENHAGEN MEETING OF THE SECOND INTERNATIONAL CONGRESS ON LIGHT

MODERN phototherapy had its beginning in Copenhagen in 1895 when Dr. Niels R. Finsen (1866–1904) demonstrated the curative effects of the ultra-violet rays from the carbon arc in healing a tuberculous skin disease called lupus. In the meantime the treatment of certain diseases by means of light rays has become world-wide.

It was therefore singularly fitting that after a lapse of almost four decades a recently established organization (Congrès International de la Lumière—biologique, physique, therapeutique) should hold its meeting in the city of the father of phototherapy and that this meeting was officered by members of the Finsen Institute; among others, including Doctors Axel Reyn, chief physician (president of the congress), Svend Lomholt, director of the laboratory, H. M. Hansen, professor of biophysics at the university, and A. Kissmeyer, the genial secretary of the second congress, through whose forethought and methodical arrangements everything pertaining to this congress functioned without a single interruption.

The purpose of the Second International Congress on Light, which met in Copenhagen on August 15 to 18, 1932, was for the presentation of reports and new data on all questions relating to biological and biophysical researches made in connection with light and the therapeutic uses of light. There was an attendance of some 300, representing 26 different countries.

The scope and the total amount of work presented at this meeting represent a long step in advance of the humble beginnings of the First International Congress (on "Actinology"), which met in Paris in July, 1929.

The Third International Congress on Light is scheduled to meet in Wiesbaden, Germany, in 1936. In view of the wide field of activities now laid out, it would appear that the next meeting of this congress may be expected to be distinguished from its

predecessors by a broad general outlook upon the future, thus expanding its usefulness, and making it more truly international in scope.

The high point in the deliberations of the Copenhagen meeting of the International Congress on Light is the recommendation to evaluate ultra-violet radiation stimuli upon a physical (radiometric) basis, in absolute units.

For this purpose the ultra-violet radiation from the source is to be separated into three components by means of a non-selective radiometer (thermopile) and a series of three standard filters. Owing to the complexity of the problem the correlation of the physical measurements with the biological and physiological (*e.g.*, erythemal) reaction is left for future settlement.

The subjects for discussion at the Copenhagen meeting were presented under four general themes: I. How can the effect of light baths on tuberculosis be explained? II. The basis and organization of helioclimatic researches in relation to public hygiene. III. The rôle of pigmentation in the biologic action of light, and the therapeutic effect of light baths. IV. The choice of a unit and a method of measuring ultra-violet radiation used in medicine.

For each of the above-mentioned themes there were one or two "rapporteurs" and 5 to 6 "co-rapporteurs"; also a leader of the "discussion." As is to be expected, these reports summarize data and information in particular fields of activity. The opinions expressed are those of the individual presenting the subject.

In addition to these papers on general subjects that had been selected in advance of the meeting of this congress, there were a large number of special communications on investigations in progress, as follows: Physics, 18; biology, 24; therapy, 11; and biochemistry, 8 papers.

One day was devoted to visiting the Finsen Institute and to the Minkerup Sanatorium. At the former institute members of the staff gave lectures on the use of phototherapy in the treatment of cutaneous, oto-laryngologic and surgical tuberculosis. In the latter institution there was a lecture on the results of seacoast sanatorium treatment of 1,400 scrofulous children.

At the conclusion of the meeting of this congress there were visits to other sanatoria in Denmark, notably the Julemaerke Sanatorium (on Kolding Fjord) and the Vejle-fjord Sanatorium.

The reports and abstracts of the communications presented at the Copenhagen meeting of the "II^e Congrès International de la Lumière" will be published in book form by Engelsen and Schroder (Copenhagen, Denmark). Readers interested in procuring a copy should address the publishers, or the Secretary General, Dr. A. Kissmeyer, Finsen Institute, Copenhagen. This publication contains over 400 pages of material which is entirely too long to even attempt to summarize in this communication.

It must suffice to record the results of the deliberations of the committee on measurement and standardization of ultra-violet radiation used in medicine. These results are summarized in the following statement (translation from French), which was presented at the concluding meeting of the congress:

In the meeting of Aug. 17th in the Castle of Christiansborg the committee after a discussion and exchange of different points of view, decided unanimously:

1. To recommend the standardization of sources used in medicine, dividing the ultra-violet spectrum in three spectral parts, defined provisionally by the following filters:

Noviol-A—Barium-flint (U. V. of long wave-length, or U. V.—*A.* giving approximately the spectral band from 4000 to 3150A).

Barium-flint—Pyrex (U. V. of medium wave-length, or U. V.—*B.* giving approximately the spectral band from 3150 to 2800A).

Pyrex (U. V. of short wave-length, or U. V.—*C.* giving approximately the rays shorter than 2800A).

These filters, made from a special melt will be given to the following national institutes:

Bureau of Standards, Washington.
Comitade Nazionale della Ricerche de Rome.
Institut d'Actinologie, Paris.
Institut Finsen, Copenhagen.
Institut für Strahlenforschung, Berlin.
National Physical Laboratory, Teddington, London.

If possible these institutes will standardize these filters for manufacturers, physicians and meteorologists.

For each part of the spectrum as defined by these filters, the measurement of the radiation is to be made radiometrically by means of a non-selective method (*e.g.*, by a thermopile) and preferably (for medical and meteorological measurements) expressed in milligram calories per cm^2 per minute.

The lamp manufacturers are advised to give energy data for these parts of the spectrum for all their lamp types, stating all conditions of measurement.

The distance from the lamp to the receiving instrument should be the one used during medical treatment, and in case the distance to the patient can be varied a distance of 1 meter is recommended.

(2) The committee recommends to physicians the use of simple physical, biological, photochemical or photoelectrical methods of measuring in order to check the constancy of each lamp used. The committee emphasizes that at the present time a comparison of intensities by such methods is only possible for lamps of the same type and not for lamps of different types.

(3) The definite adoption of a unit of measurement

for the intensity of the ultra-violet used in medicine can not be recommended at the present Congress. In view of the complexity of the biological problems which must be solved before a unit can be fixed, the International Committee proposes to undertake a program of cooperation between the different institutes to serve as a basis of discussion at the meeting of the next Congress, when this question will be considered.

(4) The committee has decided to prepare an actinometric bibliography of the papers interesting to biologists and physicians. This will be published by the secretary general of the committee on measurement and standardization, Dr. J. Saidman, in the "Annales d'Actinometrie."

(5) The present members of the International Committee of Measurement will make these recommendations known to the different medical societies and scientific journals of their respective countries. To the non-represented countries the recommendations will be sent by the secretary general of the committee.

The production of such filters as recommended will probably never be a commercial proposition. If so, the various countries will probably eventually manufacture them for their citizens. In the meantime (the experimental stage) I have been assigned the task of procuring the prompt delivery of standard samples of these filters to the national laboratories. To expedite matters, Dr. H. P. Gage, of the Research Laboratory of the Corning Glass Works, Corning, New York, has kindly undertaken to promptly supply samples from large melts of each kind of filter glass recommended for measuring the ultra-violet in the spectral bands, *A*, *B*, and *C*. The original recommendation mentioned Corex-D glass to obtain the spectral band, "C." However, since this would require a thickness of almost 4 mm, another kind of glass, Electric Pyrex (which has a sharper ultra-violet cut-off than Corex-D) will be used.

It is to be noted that the barium-flint filter gives the radiation in the spectral range of wave-lengths less than 313 millimicrons, which is of importance in erythemal and antirachitic tests. This use of a physical specification of the radiation in the bands of wave-lengths *A*, *B* and *C* avoids reference to biological effects, such as for example, erythema. This places the evaluation of the radiation stimulus upon a physical basis, hoping eventually to obtain the biological correlations when better understood.

While these recommendations specify the use of merely the filters (which will be sufficiently accurate for some work, and will be a step in advance in systematic work) nevertheless, owing to small variations in the spectral transmissions of different samples of the same kind of filter, for more precise work it will be desirable to know the relative spectral energy distribution of the source, in order to evaluate more exactly the energy in a given spectral band.

In all cases a cell of water, 1 centimeter in thickness, within thin windows of crystalline quartz, should be used in front of the thermopile to eliminate the difference in the infra-red absorption by these filters.

In order to obtain the radiation intensity of any spectral band, in absolute value, the thermopile is calibrated by exposure to a standard of radiation, such as is issued by the Bureau of Standards.

The complete accomplishments of such a congress can not be summarized in print. Naturally in an international group (some 300 in all) of biophysicists, biochemists, physiologists, biologists and phototherapists, there is bound to be a diversity of opinions and personal interests. It is to be hoped that by the next meeting the fundamental problems will be sufficiently clarified so that personal preferences can be given up and action can be taken to meet future needs.

Evidently the time was not ripe for sacrificing personal preferences and looking forward to the formulation of a definite general procedure that will be the best for the future. For example, one experimenter, using gram calories, wanted to continue to do so, partly because he is equipped for making such measurements, and partly because the gram-calory is used in metabolism—the latter a novel idea which, if adopted, may lead to much confusion. Another experimenter, equipped with a total radiation pyrheliometer for measuring the dosage intensity of solar radiation, instead of the ultra-violet component in which he was principally interested, wanted to continue to use his instrument in spite of its shortcomings. Still another worker, apparently unfamiliar with the functioning of a thermopile, was opposed to its use for measuring ultra-violet radiation because it was non-selective to wave-length: thus overlooking an important principle that permits direct standardization in fundamental units, which is not possible with selective photochemical, photoelectrical and photographic devices

The question whether the specification of the dosage should be on a physical or a correlated biological (erythemal) basis was discussed in the first congress in 1929, and again in the present meeting. But the subject is so new that the physiologists and the phototherapists, who use the erythemal test to gauge the initial dose, could not come to agreement.

In this country, the evaluation of radiation stimuli, used in physical, biological and physiological work, in energy units (microwatts per cm^2) was begun about 18 years ago. The method is now in common use, not only in recording the intensity of radiation stimuli, but also in specifying the ultra-violet output

of lamps. Hence, as far as this country is concerned, experimental procedure will continue practically as it has in the past.

As already stated the International Congress on Light is to meet again in 1936. The present indications are that, in the meantime, there will be greater international cooperation and good-will than ever before; and when the international committee on measurement and standardization again meets, those present should have ample information and data available upon the pressing questions awaiting action.

W. W. COBLENTZ,
United States member, International Committee on Measurement and Standardization; representative, Council on Physical Therapy, American Medical Association.

SCIENTIFIC APPARATUS AND LABORATORY METHODS

DETERMINATION OF THE EASILY SOLUBLE PHOSPHORUS IN SOILS

DURING the past few years several different chemical and biological methods have been proposed for the determination of the easily soluble phosphorus content of soils. Methods in which it is necessary to grow bacteria or plants in order to secure information in regard to the availability of plant food in soils are objectionable in routine analysis because of the length of time required to complete the determinations. Also it is difficult to secure the same results when these methods are used on samples of soil taken from the same area at different times of the year.

Chemical methods do not imitate the plant as far as the extraction of the phosphorus from the soil is concerned. The solvent added to the soil comes in contact with the surface of all exposed mineral phosphates; whereas the plant roots secure their phosphorus through the root hairs which come in contact with only a few phosphate particles as compared with the total number which are present in the soil. Also there is the possibility of the absorption of the dissolved phosphorus in some soils when certain extraction methods are used, which occurs to a less extent in case of the plant roots which secure the major portion of their phosphorus directly from the water film surrounding the phosphate particles.

The value of any method will depend upon the correlation which occurs between the amount of phosphorus extracted from the soil and the response secured from phosphorus fertilizers applied to crops grown on that soil under field conditions. In order to secure accurate correlations a large number of different soils must be studied and comparisons made with each crop which is grown.

As a result of an extensive investigation of different chemical methods which have been proposed for the determination of the easily soluble phosphorus content of soils, the best correlation between the response from phosphorus fertilizers applied to crops grown on different soils and the easily soluble phosphorus removed from soil was secured with the method which is described in the following paragraph. This method separates quite accurately those soils which respond and do not respond to phosphorus fertilization. A complete report of this investigation will be published elsewhere.

METHOD OF SOIL ANALYSIS

Place a heavy filter paper over one end of a glass tube which is one inch in diameter and four inches long and fasten the filter paper to the end of the tube with a rubber band. Satisfactory tubes can be made by breaking the closed end of a test-tube one inch in diameter and six inches long and smoothing the broken end of the tube with the aid of a nichrome wire gauze and a good burner. Add 10 grams of 60 mesh phosphorus-free glass sand or alundum to the tube and tap gently to obtain a level surface. Place 5 grams of pulverized soil in an even layer on top of the sand or alundum and then cover the soil with 5 or 10 grams of sand so that it will not be disturbed when the solvent is added. Place the tube in a clamp so that it is held in vertical position. Add 200 cc of tenth normal acetic acid to an Erlenmeyer flask. Place a rubber stopper containing a glass tube 8 or 9 millimeters in diameter and 2 inches long in the mouth of the flask and pour enough solution into the percolation tube to cover the sand one inch deep. Immediately invert the flask over the tube and allow the solution to percolate through the soil.

Catch the filtrate in a beaker or a flask and when the percolation is complete determine the phosphorus in a 25 cc aliquot which is placed in a 1 by 6 inch test-tube and treated as follows: Add .5 cc of seven normal sulphuric acid containing 2.5 per cent. of ammonium molybdate; mix the solution in the test-tube thoroughly; allow it to stand about one minute, and then add two or three drops of stannous chloride solution which develops a blue color if phosphorus is present. The stannous chloride solution is made by dissolving one half gram of tin in 10 cc of arsenic-free hydrochloric acid, after which it is diluted to 50 cc with distilled water.

Comparisons can be made with tubes containing known amounts of standard phosphate solution which have been diluted to a volume of 25 cc. When soils contain less than .008 milligrams of phosphorus in 25

cc of filtrate, a profitable response from phosphorus fertilization will be secured if other limiting factors are also supplied. Soils which contain from .008 to .013 milligrams of phosphorus in 25 cc of filtrate are in an intermediate zone where response from fertilization is usually slight. The soils which were studied in this experiment and contained more than .13 milligrams of phosphorus in a 25 cc aliquot did not respond to phosphorus fertilizers applied to ordinary field crops.

Some soils which are particularly deficient in easily soluble phosphorus may have a high absorptive capacity for that element when it is applied to the soil, and under such conditions crops may not respond appreciably to phosphorus fertilization. When a soil filtrate contains less than .002 milligrams of phosphorus in 25 cc, it may be desirable under certain soil conditions to determine the ability of those soils to fix large amounts of phosphorus. This can be done by leaching a soil with a solution containing a known amount of mono-potassium or mono-calcium phosphate, followed by a second leaching with 200 cc of tenth normal acetic acid. The amount of absorption can be determined by difference after subtracting the easily soluble phosphorus removed by a similar quantity of acid passing through an untreated sample of the same soil.

Tenth normal acetic acid will dissolve considerable amounts of freshly precipitated iron, aluminum and manganese phosphate; consequently in certain soils which have some calcium phosphate present in them which is available to the plant roots which come in contact with it, very little phosphorus may be extracted by distilled water, carbonated water or sodium acetate solutions, buffered to pH 4, 5 and 6, because of the absorption of the dissolved phosphorus by the soil. Under such conditions it is necessary to use a solution which is more acid than a saturated aqueous solution of carbon dioxide to keep the dissolved phosphorus from being absorbed by the soil particles. Since acetic acid will separate soils which contain all their phosphorus in the form of iron or aluminum phosphate from soils which contain varying amounts of calcium phosphate, and also has a high buffer capacity which tends to keep the reaction of the extracting solution more nearly constant for different soils, it is more desirable than other solvents which have been recommended.

The rate of percolation of a solution through a soil will depend to a considerable extent upon the texture and structure of the soil particles. In these experiments 200 cc of acetic acid percolated through the average soil in two to five hours. In case of coarse sandy soils the time required for the solvent to pass through the soil may frequently be less than thirty minutes. In case of clay soils sometimes the rate of percolation is very slow. In some instances this can be hastened by mixing sand with the soil, which may reduce the total amount of phosphorus extracted. In other instances mixing the soil with large amounts of sand will not increase the rate of percolation. If the determinations are started in the evening, in most cases the solvent will pass through the soil before morning. In case of calcareous soils in which considerable amounts of occluded phosphate occurs, the method can not be recommended. When small amounts of calcium carbonate exist in the soil, the result obtained by this method agree very well with crop yields secured from the application of phosphate fertilizers applied to the soil.

It is quite possible that plant methods might be used to good advantage on soils which are in the intermediate zone as determined by this test. In case of calcareous soils and other soils which do not absorb large quantities of phosphorus after it is brought into solution by the extracting medium, a less acid solvent could be used. This will reduce the error which may occur due to the solution of the protective coating surrounding occluded phosphates which are frequently found in calcareous soils.

When crops are planted on soils containing a large amount of organic phosphorus which is readily mineralized by bacterial action, frequently the response from phosphorus fertilization is slight, even though only small amounts of phosphorus are removed by dilute acid solutions. Under such conditions extraction of the soil with a solution containing one per cent. of sodium or potassium carbonate may be used to detect a phosphorus deficiency.

HORACE J. HARPER

OKLAHOMA A. AND M. COLLEGE

CIRCULATION AND AERATION APPARATUS FOR AQUATIC MEDIA

WITH the growing recognition of the value of fishes and fish eggs as laboratory material for physiological and embryological study[1] the problem of adequately aerating the incubating eggs becomes important. The common method used in state fish hatcheries demands a continuous flow of fresh water from sources native to the eggs used. This is obviously impossible in the average laboratory, and experience has indicated that the mortality caused by chemical content, together with a predilection toward fungi, when flowing city water is used, is too high to make the method practical. The following easily constructed apparatus overcomes these difficulties.

The container is a quart milk bottle (see Fig. 1). Paraffin is melted in the bottom of the bottle to form a layer about ¾″ in depth. While this is cooling two

[1] Floyd J. Brinley, "Eggs of Fresh-Water Fishes Suitable for Physiological Research," SCIENCE, 74: 295-296, 1931.

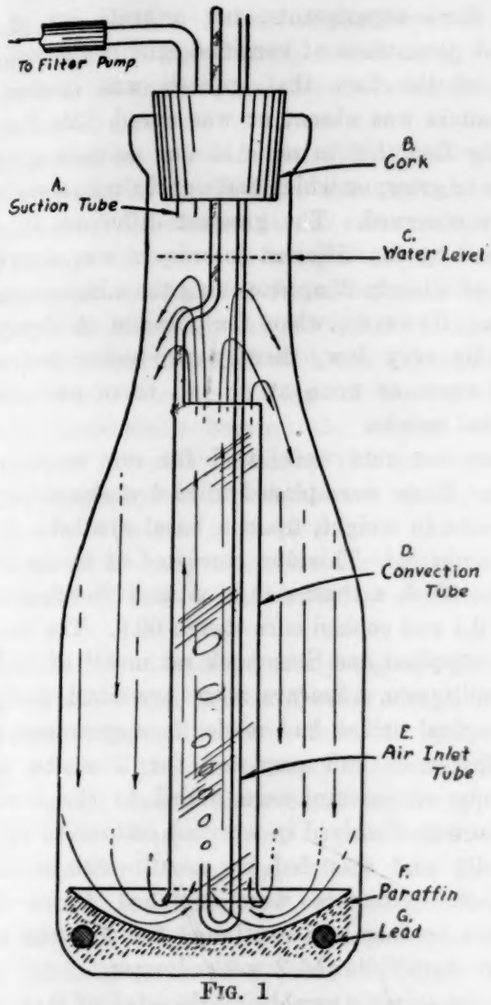

FIG. 1

10 gram pieces of lead are embedded near the lower margin of the paraffin to overcome its tendency to float, in the absence of a perfect seal at the periphery. When cooled it is made cup-shaped with a flame provided by connecting a glass tube, drawn to a tip, to a gas jet. By repeatedly melting the center of the paraffin, and slowly revolving the inclined bottle to allow the melted portion to build up on the sides, the desired cup is obtained. When hard, this can be fire-polished smooth by lightly passing the flame over the surface. The well, thus formed, serves to direct the eggs under the mouth of the convection tube.

The convection tube (D) is made from a 1″ test-tube 6″ long, from the bottom of which 1″ is cut. A $\frac{1}{8}$″ glass rod 6″ long with a $\frac{1}{2}$″ double bend about $\frac{3}{4}$″ from one end is fused by its short section to the cut end of the convection tube, so that when the long section is inserted in the cork the line of suspension is vertical and along the axis of the convection tube. The working distance of this tube is about $\frac{1}{2}$″ above the paraffin, varying with the size of the eggs and the amount of circulation desired. The air inlet tube (E) is $\frac{1}{8}$″ glass tubing 14″ long with a $\frac{3}{8}$″ U bend $\frac{1}{2}$″ from one end. This is suspended inside the convection tube so that the air jet is in the center. The suction tube (A) is $\frac{3}{4}$″ glass tubing 5″ long with a right angle bend in the middle. The cork (B) is drilled in the center to accommodate the convection tube rod, and $\frac{1}{4}$″ along a diameter on each side of the center to accommodate the inlet and suction tubes. The apparatus is set up as shown in the figure (all unions being air-tight) and attached to a filter pump.

When in operation the suction, created by the jet of air passing through the convection tube from the air inlet, will circulate the eggs up through this tube, discharging them at the top; they will then be carried to the bottom of the bottle by gravity and the current, where they will again be drawn up into the convection tube (circulation indicated on figure). The entire medium is filled with moving eggs, which are constantly suspended in the highly oxygenated water. The volume of air passed through, and the relationship of the inlet tube to the bottom of the convection tube, determine the velocity of the current. Dr. Floyd J. Brinley, of this department, has found the apparatus highly successful for the incubation of eggs of the wall-eyed pike (*Stizostedion vitreum*) with respect to percentage and speed of hatching. About 20,000 eggs can be handled in each bottle.

Since the apparatus permits control of temperature, aeration and circulation, thus maintaining a uniform medium under ordinary laboratory conditions, it lends itself readily to many problems involving effects of temperature, chemical solutions, gases, etc., on aquatic organisms. It may be useful in chemical problems utilizing solutions and precipitates. Modifications of the idea also suggest themselves for many problems; for example, the efficiency of the apparatus described by J. Henry Walker, Jr., in SCIENCE for June 26, 1931 (method for oxygenating an aquarium), can be increased by the addition of the convection tube about the air intake. The current created carries air bubbles down into the medium, permitting greater diffusion.

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SPECIAL ARTICLES

THE VAGINAL SMEAR METHOD OF DETERMINING VITAMIN A[1]

IN the quantitative determination of vitamin A,[2] three different biological methods have been used. These are what may be called the growth method, the ophthalmic method, and the vaginal smear method.

[1] From the Laboratory of Agricultural Chemistry, University of Wisconsin, Madison, Wisconsin.

[2] In this paper "vitamin A" refers to all substances which show vitamin A activity.

The growth method, which was the first one used, depends upon the fact that when a young animal is deprived of vitamin A, it ultimately ceases to grow, and when it is fed vitamin A in sufficient amounts, its growth is resumed. The amount of growth obtained under standard conditions is taken as an index of the amount of vitamin A present. The ophthalmic method takes advantage of the fact that when rats are kept on a diet deficient in vitamin A they ultimately develop ophthalmia, which is cured rapidly by the administration of sufficient amounts of vitamin A. The ability or failure to effect a cure, or even the rate of cure under standard conditions, has been used as the quantitative index. The vaginal smear method is based on the observation of Evans,[3,4] who noted that rats on a vitamin A deficient diet showed a persistence of cornified cells in the vagina, and that the addition of large amounts of vitamin A caused a quick resumption of the normal smear picture. He suggested that this fact be used as a method of testing for vitamin A, but he did not compare his results with those obtained by other methods. This was done in 1929 by Coward[5,6] and associates, who reported the vaginal smear method unsatisfactory for general use.

In 1930, however, Schmidt and Schmidt[7] successfully used this method in determining the absorption of vitamin A in the absence of bile. Since then the vitamin A activity of carotin has been established on a quantitative basis, and one gamma (.001 mg) of the same has been accepted as the international unit. By its use, it is now possible to feed constant amounts of active material in all laboratories and to observe the resultant physiological response. We have accordingly compared the sensitivity of the growth method, the ophthalmic method and the vaginal smear method to uniform dosage with carotin as the source of vitamin A.

For our preliminary observations we used rats which had been started on other experiments designed to determine the effect of additions of carotin, egg yolk, liver or burbot oil at various levels to a diet low in vitamin A. These rats were examined by the vaginal smear technique of Evans, and the smear results were compared with the growth of the animal and the rate of cure of ophthalmia. Smears were also run on animals being depleted of their vitamin A stores, and similar comparisons made.

In these experiments, ten animals out of sixty showed persistence of cornified cells in the vagina, in spite of the fact that growth was resumed and ophthalmia was absent or was cured. Most striking was the fact that in none of our animals which had ceased to grow, or which had ophthalmia, were normal smears observed. The greatest difference in results obtained by the different techniques was observed on levels of vitamin A approaching the minimum requirements. However, when the vitamin A dosage was high, or very low, thereby producing respectively rapid cures or none at all, all three methods gave identical results.

Forty-five rats were used for our major experiments. These were placed when 4 weeks old, at 50 to 60 grams in weight, upon a basal synthetic diet low in vitamin A.[8] This diet consisted of casein 18, agar 2, salts 40[9] 4, a yeast rich in vitamin B 6.9, irradiated yeast 0.1 and cooked corn-starch 69.0. The irradiated yeast supplied one Steenbock rat unit[10] of vitamin D per milligram. Smears were examined daily after the vaginal orifice had made its appearance. After cornified cells had persisted for 2 weeks, varying amounts of carotin were added to the diet. The carotin was dissolved in purified cottonseed oil (Wesson oil) and was fed by mouth with a medicine dropper. Animals were weighed thrice weekly. Carotin feeding was continued for 5 weeks and the smears were followed 2 weeks longer.

As the animals were being depleted of their vitamin A reserves, the first sign of the deficiency was a continuation of cornified cells in the vagina, the smear picture otherwise being identical with that of normal oestrum. This phenomenon has been reported by Evans and others. After 2 or 3 weeks, however, a more marked deterioration of the vaginal epithelium manifested itself. The cells became more necrotic with the accumulation first of débris and later of colloidal materials as well. Occasionally leucocytes reappeared, sometimes in large numbers, but the colloidal cloudy material present rendered it relatively easy to distinguish between these smears and those of normal dioestrum. Time and again typical cornified cells appeared at intervals, as well as combinations of cornified cells and leucocytes. In other words, the vaginal smear of a vitamin A deficient rat at first revealed a picture of a mass of persisting typical cornified cells and later a mass of débris, alternating in variable sequence with leucocytes plus débris, cornified cells plus débris, true cornified cells or leucocytes plus

[3] H. M. Evans and E. S. Bishop, *Jour. Med. Res.*, 1, 335, 1922.
[4] H. M. Evans, *Jour. Biol. Chem.*, 77, 651, 1928.
[5] K. H. Coward, *Jour. Physiol.*, 67, 26, 1929.
[6] K. H. Coward, B. G. E. Morgan, F. J. Dyer, *Jour. Physiol.*, 69, 349, 1930.
[7] W. Schmidt and C. L. A. Schmidt, *Univ. Calif. Pub. Phys.*, 7, 211, 1930.
[8] H. Steenbock, M. T. Nelson and A. Black, *Jour. Biol. Chem.*, 62, 275, 1924.
[9] H. Steenbock and E. M. Nelson, *Jour. Biol. Chem.*, 56, 355, 1923.
[10] H. Steenbock, S. W. F. Kletzien and J. G. Halpin, *Jour. Biol. Chem.*, 97, 249, 1932.

cornified cells. This latter appearance, if the deficiency remained uncorrected, lasted until death. Either or both of these types of smears were designated as "low A smears."

In rats placed on a low A diet at 50 to 60 grams and at an age of 22 to 25 days, the vaginal orifice usually makes its appearance in our colony at an age of 39 to 84 days—the average being 53 days. Within this range, no correlation was found between the age at maturity and the height of the animal at the beginning of the experiment. But it was impossible to use all our female rats for the vaginal smear-growth-ophthalmia correlations because the vaginal orifice frequently was not established by the time growth had ceased or ophthalmia had developed. As a matter of fact, out of one group of 45 rats on the low A diet, 9 remained sexually immature during the course of the experiment and 3 matured after cessation of growth.

Rats on the low A diet generally showed "low A smears" before the appearance of other symptoms of the deficiency, although in some cases all symptoms appeared at about the same time. However, in no case were normal smears observed after the appearance of other low A symptoms. Again referring to the previously mentioned group of 45 rats, 22 per cent. showed low A smears and stopped growing at the same time, 18 per cent. showed low A smears 3 to 7 days before stoppage of growth, and 33 per cent. showed low A smears 7 to 14 days before cessation of growth. As far as ophthalmia and growth are concerned, the majority of our rats stop growing at the time the ophthalmia makes its appearance and *vice versa*.

The different symptoms of vitamin A deficiency were found to respond unequally to carotin administration, Table 1. On 3 to 5 γ carotin per day the general tendency was for the ophthalmia to be cured and slow growth to continue for five weeks without restoration of the normal smear picture. The addition of 10 γ or more of carotin per rat per day restored dioestrous smears within a week, and oestrum in two weeks.

As a result of our experience we have come to the conclusion that the vaginal smear method can be used as a quantitative method for the determination of vitamin A. It has the following desirable features:

(1) The response to the addition of vitamin A is rapid—generally within a week.

(2) The amount of vitamin A necessary for a positive response is definite.

(3) Animals of various ages, even older animals as discards from other experiments, can be used and one animal may even be used repeatedly.

(4) Like the cure of ophthalmia the reaction is specific, but unlike ophthalmia the reaction is not so complicated and, therefore, more reliable. Needless to say it is far more specific than growth.

(5) The test can be used to determine vitamin A sufficiency in experiments with adult females without introducing complications.

TABLE I

COMPARATIVE CORRECTION OF SYMPTOMS OF VITAMIN A DEPLETION BY DIFFERENT AMOUNTS OF CAROTIN

Carotin given daily	Lot	No. of rats	Growth in 5 weeks	Condition of eyes after 5 weeks	Condition of smears after 5 weeks	Remarks
gamma			*gms.*			
3	179	4	15	Cured	Not cured	Slight swelling of eyelids cured in 10 days
		2	22	"		Immature
5	180	4	27	—	Not cured	
		1	23	—	Cured	Normal smears restored in 4 days
	173	2	35	Cured	Not cured	Swelling of eyelids cured in 1 week
		1	40	—	Cured	Normal smears restored in 4 days
10	174	1	40	Cured	"	Low A smears for 23 days before cure—eyes purulent when carotin was added
		5	35	"	"	2 rats showed swelling and bleeding of eyelids; cured in 1 week—Normal smears within 1–7 days
	176	1	25	—	Not cured	Low A smears reappeared after third week
		3	41	Cured	—	Matured 2 weeks after carotin addition . . . smears normal
20	175	4	41	—	Cured	Normal smears restored in 2–4 days
	177	6	36	Cured	"	Normal smears restored in 1–8 days—swelling of eyelids cured within a week
40	178	4	50	"	"	Normal smears restored in 1–4 days

The following features operate against its general use:

(1) It requires considerable routine work.

(2) Only female rats can be used.

(3) Many females fail to mature sexually on a vitamin A deficient diet before they succumb to other symptoms and therefore can not be used.

(4) It is less sensitive than growth or the cure of ophthalmia for the detection of small amounts of vitamin A, *i.e.*, it takes more carotin to restore normal smears than to restore growth or to cure ophthalmia. For quantitative work this objection is not serious, since the amount of carotin (10 to 20 γ) necessary for normal smears is quite as definite as the amount (5 to 10 γ) necessary for growth, or the amount of (3 to 5 γ) necessary for a cure of ophthalmia.

(5) Like the ophthalmic method it is difficult to express the results in numerical terms. In this respect growth or maintenance in weight has obvious advantages, if one can be certain that all dietary requirements other than vitamin A have been supplied by the basal ration.

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H. STEENBOCK

CHEMICAL CHANGES IN THE BLOOD IN ADDISON'S DISEASE[1]

THE significance of the loss of inorganic base from the body in diabetic acidosis, in cholera and in diarrhoeas of infancy, in high intestinal obstruction and in terminal chronic nephritis is now thoroughly appreciated. All these pathological states are characterized clinically by severe prostration, dehydration, lowering of the serum chloride concentration, nitrogen retention and frequently by a decrease in the bicarbonate concentration of the blood and "shock." Since these changes are also typical of the disease picture of severe adrenal insufficiency, we have studied in detail the electrolyte structure of the blood in three patients suffering from Addison's disease.

In the accompanying table it will be seen that all three patients showed deviations from the normal which were qualitatively similar. Of particular interest is the decrease in total base which occurs entirely at the expense of sodium, because in all three cases the potassium content of the serum was either at a "high normal" level or definitely increased. The changes observed in chloride, bicarbonate, non-protein nitrogen and blood sugar concentrations are those already well known. The retention of inorganic sulphate probably accompanies that of non-protein nitrogen. The abnormalities of the blood found in our patients suffering from Addison's disease are similar to the unpublished results attained by Zwemer in his study of adrenalectomized cats.

The loss of sodium and the increase in potassium in the blood serum of the patient E. C. is striking. This patient received two injections of extract of adrenal cortex prepared by Dr. R. Zwemer before the blood study was made and two injections later, but died in spite of this therapy. The patient J. V. was well except for increasing pigmentation of the body and buccal mucous membranes and for occasional vomiting spells for four months preceding admission to the hospital. In this patient, the decrease in the serum sodium concentration is also definite, but less marked than in the case of E. C. The blood of the third patient, M. W., was examined on three occasions. On admission the patient was markedly prostrated and, as in the other cases, showed a significant decrease in

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BLOOD CHANGES IN ADDISON'S DISEASE

Name	Date	T.B.	Na	K	Ca	Cl	HCO_3	PO_4	SO_4	Prot.	NPN	Sugar	Haematocrit	Blood pressure	Remarks
		me.q. p.l.	me.q. p.l.	me.q. p.l.	me.q. p.l.	me.q. p.l.	me.q. p.l.	me.q. p.l.	me.q. p.l.	me.q. p.l.	mgm. per 100 cc	gm. p.l.			
E. C.	5– 9–32	127.7	109.5	8.74	6.6	70.1	18.0	4.3	4.0	18.2	75.9	0.72	44.4	76/52	Received 4 injections of Adrenal Cortex (Zwemer). Died on 5–11–32.
J. V.	5–17–32	144.9	131.3	5.3	5.4	97.6	26.1	1.9		17.0	32.0	0.91	41.7	102/60	
M. W.	7–19–32	136.3	123.5	5.3	5.3	88.6	21.8	2.6	2.3	15.1	39.0	0.73	42.0	85/55	
M. W.	7–26–32	125.8	107.8	7.1	4.8	72.7	21.5	2.4		16.9	45.0	0.80		65–70/48	Received 10 cc. of Eschatin on 7–26.
M. W.	8– 2–32	147.5	133.0	5.1	5.9	93.8	27.5	2.6		13.5	20.6	1.20	31.4	84/60	Patient had received 12–15 gm NaCl daily for 6 days.

sodium concentration in the blood serum. During the next week her condition became critical and the concentration of sodium fell still further to a level of 107.8 m.eq. per l. and the potassium rose to 7.1 m.eq. She was given only one injection of 10 cc of "Eschatin," a commercial preparation of adrenal cortex substance, intravenously and then received 12 to 15 gms of NaCl daily. It is interesting to note that after one week of NaCl administration the patient became almost entirely symptom-free and that simultaneously the abnormalities of her blood practically disappeared.

The mechanism of base loss in Addison's disease is not clear, but seems to be intimately related to the clinical picture of adrenal insufficiency and is being studied at the present time. It seems possible that the symptom complex may in part depend upon the profound changes in the relative concentrations of sodium and potassium. Whether or not the replacement of base in the patient M. W. was responsible for the amelioration of symptoms can not be stated, but the improvement which has persisted for two months with forced NaCl administration is impressive.

In conclusion, it may be stated that the clinical picture of severe adrenal insufficiency in many respects simulates that of other disease conditions, in which the loss of inorganic base plays an important rôle. Furthermore, a definite decrease in the sodium content of the blood serum, with a simultaneous tendency for potassium to increase in concentration, has been observed in three cases of Addison's disease. The patient treated with large doses of NaCl showed striking clinical improvement with the reestablishment of a more normal electrolyte structure in the blood serum.

ROBERT F. LOEB

HEREDITARY VARIATIONS IN THE SKULL OF THE RABBIT

THE skull of the rabbit presents a group of striking hereditary variations, including two distinctive types which may be designated as *dome* and *ridge* skulls. The exact mechanism of inheritance of these conditions has not been determined with certainty, but, so far, more than 500 skulls have been studied and a brief summary of the results may be given.

Dome and ridge skulls appear to be expressions of the combined action of a group of unit factors which affect the size and shape of individual bones, the number of bones, suture patterns and the character and angle of bony union with the bregma, the coronal and sagittal sutures as visible foci of action. The bones chiefly affected are the frontals and parietals.

Considered individually, the variations concerned may be designated as "reversed suture," "accessory bone" and "fused suture." These conditions are present at birth and with continued growth of the skull lead to or become associated with other structural alterations.

In general, the coronal and sagittal sutures of the rabbit intersect at right angles or the coronal dips forward to form a slight V. In the typical "reversed suture," the coronal turns posteromedially at some distance from the bregma to intersect the sagittal in its middle third. The size and shape of the frontal bone is thus altered and the parietal correspondingly affected.

The condition described as "accessory bone" is one in which a supernumerary bone is produced by the formation of an accessory suture extending from the coronal to the sagittal suture. This suture usually follows a course similar to that of a reversed suture giving the resulting bone a roughly triangular shape. Rarely an accessory bone is found with a disproportionately long sagittal border in which case the accessory suture branches from the sagittal and runs close to and parallel with it to intersect the coronal a short distance from the bregma. The course of the coronal is often modified, its junction with the sagittal lying some distance anterior to that of the opposite side, so that the accessory bone lies partly in the frontal and partly in the parietal area.

The term "fused suture" has been applied to a condition in which the serrated markings of the suture and even the line of demarcation between bones are largely or entirely obliterated and, on the outer surface of the skull, are replaced by a smooth overgrowth of bone which creates the visual impression of continuity; in reality, the bones are still separable. The sutures affected by this change are mainly the coronal and sagittal.

The conditions described occur as unilateral or bilateral variations and in various combinations, symmetrical or asymmetrical. Individually, they produce comparatively little alteration in the general appearance of the skull, but, in combination, profound modifications of form and size are produced.

The ridge skull results from variations affecting the sagittal suture and the parietal bones. In the normal skull, the slope of the parietals as they approach the sagittal suture is very gradual and the upper face of the calvarium is comparatively flat. In the ridge skull, however, the parietals unite at an angle and their line of union, the sagittal suture, is fused. The vertical distance between the sagittal and squamosal sutures is increased and the vertex falls posterior to the bregma. Fusion of the sagittal is most pronounced in the region between the parietal bosses where normally its denticulations are widest. Parietal bosses are small but distinctly outlined and lie close to the sagittal suture. The antero-posterior arch of

the parietals is increased and the plane of the interparietal bone and the supraoccipital portion of the occipital bone is more vertical than normal. Reversed sutures and accessory bones may occur in combination with the ridge condition.

The conformation of the skull is extensively altered in the dome variation. The vertex of the normal skull is in the frontal suture between the frontal eminences and, posterior to it, the slope of the calvarium is continuous except for a slight depression at the bregma. In the dome skull this slope is interrupted by the angular union of frontals with parietals, and the vertex is at the bregma. Frontal eminences are absent and the posterior supraorbital processes show a marked lateral curvature with their extremities in contact with the anterior tips of the temporal lines. Parietal bones are flattened with inconspicuous bosses and form more posterior walls than roofs of the cranial cavity. The plane of the interparietal bone and the supraoccipital portion of the occipital bone is less vertical than normal.

Particularly interesting is the skull possessing both ridge and dome features. The sagittal and coronal sutures are fused, and the angular union of parietals and of parietals with frontals produces a sharp raised peak, the apex of which is formed by the bregma. Parietals are extremely flattened and may be slightly concave. The inclination of the interparietal and supraoccipital bones does not differ appreciably from the normal. This is the peak skull.

When unilateral, the dome condition causes a complete loss of symmetry and a bending of the whole skull toward the affected side. The parietal and frontal bones are shorter and the nasal bone longer in antero-posterior extent on the dome side, and the arches of the normal side are accentuated. The sagittal and frontal sutures, instead of forming a straight line between the lambda and nasion, describe a curve convex toward the normal side. The contour of the interparietal bone is definitely changed, the portion on the affected side being much larger than that on the normal side. The position of the bone is also altered, its plane facing posterolaterally rather than directly posterior as in the normal skull. The cutting edge of the upper incisor teeth is sloped due to a gradual shortening toward the dome side. Fusion of the sagittal suture may occur, causing increased flattening of the parietal on the dome side and decrease in the arch of the other. A reversed suture or an accessory bone may occur opposite a unilateral dome. Both of these combinations increase the distortion and accentuate the lateral curvature of the skull.

While these descriptions deal largely with the calvarium, it may be pointed out that the base of the skull and the cranial cavity are subjected to alteration and there is some evidence to indicate that the brain may be affected by these changes.

With reference to the inheritance of this group of skull variations, the conditions described as "reverse suture," "accessory bone" and "fused suture" are inherited as distinct entities. They show some variation in expression, but, in general, they are recessive to the corresponding normal condition and are either definitely expressed or absent. They are also differentiated into right and left sided characters, as indicated above, and may occur in any combination with normal characters or with other variations, but certain combinations are of more frequent occurrence than others.

The precise combination of genetic factors which produces the ridge, dome and related forms of skull is still uncertain. The typical ridge skull is comparatively rare and little is known concerning its breeding characteristics. The dome skull, from which all other variations have been derived, does not breed true in all cases, and the series of characters derived from one parent by hybrid matings may differ in some respect with those derived from another. The problem is further complicated by the wide-spread presence of factors for one or more of the characters concerned in the production of the more complex types. The implications of these findings are clear.

Genetically, the importance of the observations recorded lies in the fact that a profound variation in the form of the skull can be transmitted, unaltered, from parent to offspring; by crossing an animal possessing a skull of this type with a normal, the original variation can be resolved into a group of component parts which bear little or no resemblance to the original condition, but these are inherited as distinct entities; they are differentiated into right and left sided characters and can be recombined to form the parental type as well as new types which are capable of further transmission.

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